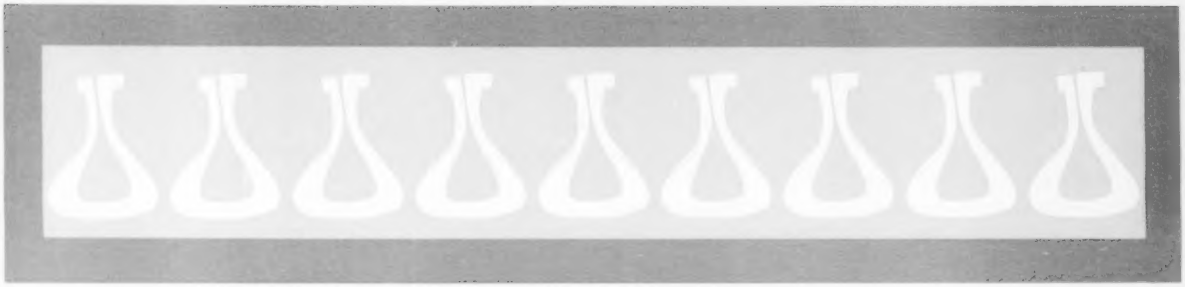

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VOL. 12 NO. 3 January 1975

PSYCHOPHARMACOLOGY ABSTRACTS

NATIONAL INSTITUTE OF MENTAL HEALTH

PSYCHOPHARMACOLOGY ABSTRACTS is a publication of the National Clearinghouse for Mental Health Information of the National Institute of Mental Health. It is a specialized information medium designed to assist the Institute in meeting its obligation to foster and support laboratory and clinical research into the nature and causes of mental disorders and methods of treatment and prevention. Specifically, this information service is designed to meet the needs of investigators in the field of psychopharmacology for rapid and comprehensive information about new developments and research results. For information or correspondence with the National Institute of Mental Health concerning *Psychopharmacology Abstracts*, changes of address, or removal of names from the mailing list see the inside back cover page.

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ABSTRACTS

PRECLINICAL PSYCHOPHARMACOLOGY

01 CHEMICAL SYNTHESIS, ISOLATION AND CHARACTERIZATION

182444 Manian, Albert A. Psychopharmacology Research Branch, NIMH, Rockville, MD **NIMH-sponsored chemical synthesis program.** Psychopharmacology Bulletin. 10(1):51-60, 1974.

A chemical synthesis program established by the National Institute of Mental Health to provide investigators with research compounds unavailable for preclinical or infrahuman studies in the area of mental health is described. The program, which was established in 1959, has been successful in fostering mental health research through directly supplying chemical entities not commercially available. As a consequence, many of the significant compounds have been made available commercially by Regis Chemical Company. Program operating procedures are outlined, 286 compounds synthesized are listed, and a bibliography of contract related and compound related publications is presented. 95 references.

182445 Craig, John C. University of California, San Francisco, CA **Synthesis of compounds related to lysergic acid.** Psychopharmacology Bulletin. 10(1):61, 1974.

Synthesis and evaluation of compounds related to lysergic acid and nitrogenous organic compounds are reported. Pharmacological activity of these new compounds is undertaken to discover their structure action relationship and identify modes of action. The goal is the discovery of compounds which may be useful therapeutic agents without the harmful side-effects of lysergic acid diethylamide (LSD).

182446 Sam, Joseph. University of Missouri, University, MS **Potential psychotropic quinolizidines.** Psychopharmacology Bulletin. 10(1):63, 1974.

Advanced biochemical techniques, including stereochemistry, were used to study the structural properties of various quinolizidine drugs, and behavioral responses of these substances were studied in cats. Preliminary results included snythesis of a number of drugs, determination of structural characteristics and toxicity data. Two variations of the 2-hydroxy-2-phenylquinolizidines showed marked analgesic activity. The systematic study of the behavioral and psychological activity associated with various chemical structure may identify the psychoactive and hallucinogenic potential in certain compounds. 0

182626 Saito, Sadakazu. Dept. of Legal Medicine, Okayama University Medical School, Okayama, Japan **Isolation and identification of hypnotics (8): isolation and identification of Benzalin and Cercine by thin layer chromatography in vitro.** Japanese Journal of Legal Medicine (Tokyo). 25(5):402-408, 1971.

Isolation and identification of two benzodiazepine derivatives in vitro by thin layer chromatography (TLC) are reported. Tests on Benzalin and Cercine indicate that it is possible to isolate and identify each of these hypnotics distinctly by TLC. However, both of the substances are apt to undergo hydrolysis in the presence of water. 9 references.

183406 Pullman, B.; Courriere, Ph.; Berthod, H. Institut de Biologie Physico-Chimique, associe au C. N. R. S., rue Pierre et Marie Curie, 75005 Paris, France **Molecular orbital studies on the conformation of hallucinogenic indolealkylamines and related compounds. The isolated molecules and the solvent effect.** Journal of Medicinal Chemistry. 17(4):439-447, 1974.

Molecular orbital studies on the conformation of hallucinogenic indolealkylamines and related compounds are reported. Conclusions about the preferred conformation(s) for serotonin can be reached by extending the computations to a larger number of indolealkylamines provided that the molecules are divided into subgroups corresponding to their possible occurrence in neutral or cationic species with an amino or dimethylamino terminal grouping. Each subgroup has its conformational preferences with respect to the two principal torsion angles. The study accounts for the X-ray crystal conformation of the representatives of the two different groups. An exception was the planar extended structures observed for the two cationic species. Evaluation of the effect of water on the conformation of the cationic forms of indolealkylamines was made by determining the principal hydration sites of the molecules. Results indicate that the hydrated cations should not manifest any marked tendency for an exclusive conformation and should exist in solution as a nearly equivalent mixture of cis and trans forms. 33 references. (Author abstract modified).

183518 Absava, G. I.; Vysotskaya, N. B. Institute of Pharmacology, Moscow **/The effects of psychic stimulants on the activity of potassium and sodium ion stimulated ATPase in the microsomal fractions of the brain of rats./** Vliyaniye psikhostimulyatorov na aktivnost' ATF-azy, stimuliruyemoy ionami Na i K, vo fraktsiyakh mikrosom golovnogo mozga krys. Farmakologiya i Toksikologiya (Moskva). 36(4):403-404, 1973.

The influence of psychostimulating agents on the activity of potassium and sodium ion stimulated ATPase in microsomal fractions of different rat brain regions was studied. Phenamine in doses of 2.5mg/kg and pyridol in doses of 12.5mg/kg were found to activate the enzyme in the diencephalon and middle brain. Caffein (25mg/kg) inhibited the transport ATPase in the microsomal fractions of the cortex. 11 references. (Journal abstract)

183520 Bardakhch'yan, E. A.; Vorontsov, V. A.; Naumov, N. N. Department of Pathological Physiology, Rostov Medical Institute, Rostov USSR **/The action of nembutal on the ultra architectonics of the neurohypophysis./** Vliyaniye nembutala na ul'traarkhitektoniku neyrogipofiza. Farmakologiya i Toksikologiya (Moskva). 36(4):419-420, 1973.

The effect of nembutal on the ultra architectonics of the neurohypophysis was studied. Intravenous administration of 20 to 30mg/kg of nembutal does not produce any changes of pituicyte organellae and neurosecretory axones as seen by electron microscopy of the posterior lobes of dogs. Individual cases of axones and terminals containing almost none of the elementary neurosecretion granules were found. A moderate liberation of neurohormones was evidenced by a small number of empty vacuoles and the absence of synaptic vessels within the zone of nerve and vessel contacts. 6 references. (Journal abstract modified)

183600 Taha, A. M.; Omar, N. M.; Bayomi, S. M.; Ammar, E. M.; Afifi, A. Pharmaceutical Chemistry Department, Faculty of Pharmacy, University of Assiut, Assiut, Egypt **Synthesis**

and screening of cyclic benzylhydrazine congeners as antidepressants. Journal of Pharmaceutical Sciences. 63(3):395-398, 1974.

Several 2-pyrazolinium salts and their corresponding pyrazolidines, congeners of a cyclic benzylhydrazine structure, were synthesized and their pharmacological activity as antidepressant agents was evaluated. The 2-pyrazolinium salts were obtained through the interaction of 1,2-dimethylhydrazine dihydrochloride, paraformaldehyde, and the appropriately substituted aralkyl ketone via a Mannich reaction. The corresponding pyrazolidines were synthesized by reduction of the pyrazolinium perchlorates with sodium borohydride in aqueous medium. The antidepressant activity of both series was evaluated in mice in comparison with nialamide. As indicators of antidepressant action, use was made of the antagonism of reserpine induced ptosis and the antagonism of reserpine protection against amphetamine lethality in mice. The possible correlations between structure and antidepressant activity are suggested. 18 references. (Author abstract)

183602 West, Norman R.; Rosenblum, Marcus P.; Sprince, Herbert; Gold, Simon; Boehmes, Diethelm H.; Vogel, Wolfgang H. Department of Pharmacology, Thomas Jefferson University, Philadelphia, PA 19107 **Assay procedures for thioridazine, trifluoperazine, and their sulfoxides and determination of urinary excretion of these compounds in mental patients.** Journal of Pharmaceutical Sciences. 63(3):417-420, 1974.

Assay procedures for thioridazine, trifluoperazine, and their sulfoxides are described which are rapid, simple, and relatively specific. Chlorpromazine interfers with the determination of these drugs whereas imipramine, desipramine, biperidin, and haloperidol do not. The urinary concentrations of these four compounds were determined in 24 hr samples and timed interval collections obtained from patients with schizophrenic reactions. Thioridazine and trifluoperazine seem to be extensively metabolized, and less than 1% of the unchanged drugs and 2-6% of the corresponding sulfoxides were observed in 24-hr urine samples. The ratio between the parent drug and its respective sulfoxide was fairly constant. Urinary excretions of thioridazine and its sulfoxide were dose independent, whereas those of trifluoperazine and its sulfoxide showed a strong dose dependency. Timed interval collections during an 8 hr period showed rather consistent excretions of unchanged trifluoperazline and thioridazine but wide intra and interpatient variations in the sulfoxide excretions. 10 references. (Author abstract)

185032 Hester, Jackson B., Jr.; Rudzik, Allan D. Upjohn Company, Kalamazoo, MI 49001 **Benzodiazepines. 4.2-Oxyamino-5-phenyl-3H-1,4-benzodiazepines.** Journal of Medicinal Chemistry. 17(3):293-295, 1974.

The preparation of a series of 2-oxyamino-5-phenyl-3H-1,4-benzodiazepines by the reaction of oxyamine derivatives with 1,3-dihydro-5-phenyl-2H-1, 4-benzodiazepine-2-thiones is described. The hydroxyamine derivative was more potent than the methoxy derivative which in turn was more active than compounds with larger substituents; the benzyloxy derivative had little activity. The oxadiazole was less active than the acyclic hydroxyamine derivative. In the present series, an o-chloro substituent on the 5-phenyl moiety markedly enhances the biological activity. This effect was particularly apparent in tests which are believed to indicate potential antianxiety activity in man. Experimental compound 14 was as active as diazepam in the nicotine, thiosemicarbazide, pentylenetetrazole, and footshock tests. The results suggest that compound 14 (U-31,920) will be an effective antianxiety drug with low sedative and muscle relaxant potential. 13 references.

185034 Sternbach, Leo H.; Sancilio, Fred D.; Blount, John F. Chemical Research Department, Hoffmann-LaRoche Inc., Nutley, NJ 07110 **Quinazolines and 1,4-benzodiazepines.64.Comparison of the stereochemistry of diazepam with that of close analogs with marginal biological activity.** Journal of Medicinal Chemistry. 17(3):374-377, 1974.

The stereochemistry of diazepam was compared with that of close analogs with marginal biological activity. It was found that two compounds are more closely related, structurally and conformationally, to diazepam than diphenylhydantoin. Nonetheless, the three benzodiazepines exhibit marked differences in their anticonvulsant properties. These findings show that conformational similarities of molecules do not necessarily indicate similar biological properties. Many other factors, many still unknown, play an important role in the biological activity of chemical entities. 9 references.

185035 Agarwal, V. K.; Chaturvedi; A. K.; Gupta, T. K.; Parmar, Surendra S; De Boer, Benjamin. Dept. of Pharmacology and Therapeutics, King George's Medical College, Lucknow University, Lucknow 3, India **Anticonvulsant activity of substituted indolealkylamines.** Journal of Medicinal Chemistry. 17(3):378-380, 1974.

The anticonvulsant activity of substituted indolealkylamines is correlated with their ability to inhibit NAD dependent oxidations by rat brain homogenates. All indolealkylamines were found to exhibit anticonvulsant activity. Six of nine compounds tested selectively inhibited NAD dependent oxidation of l-glutamate, beta-hydroxybutyrate, alpha-ketoglutarate, and pyruvate. Oxidation of succinate remained unaffected in all cases. No clear correlation was observed between the anticonvulsant activity and selective inhibition of NAD dependent oxidations of these indolealkylamines. 17 references.

185978 Kohl, H.; Desai, P. D.; Dohadwalla, A. N.; de Souza, N. J. Research Centre, Hoechst Pharmaceuticals Limited, Bombay 400 080, India **Synthesis and CNS activity of 3-substituted 7-chloro-5-phenyl-1,3,4-benzotriazepin-2-ones.** Journal of Pharmaceutical Sciences. 63(6):838-841, 1974.

Several new 3-substituted 7-chloro-5-phenyl-1,3,4-benzotriazepin-2-ones were synthesized from appropriate 5-chloro-2-aminobenzophenone hydrazones by condensation with phosgene or treatment with chloroformic acid esters and subsequent cyclization. In an evaluation of their central nervous system depressant properties, all of the compounds exhibited mild depressant and anticonvulsant activity which was only marginally influenced by the 3-substituent. 19 references. (Author abstract)

185979 Data, John B.; Taylor, Michael L.; Forcione, Mario. Dept. of Medicinal Chemistry - Pharmacognosy, School of Pharmacy and Pharmacal Sciences, Purdue Univ., West Lafayette, IN 47907 **Preparation and pharmacological screening of indanethylamines related to tryptamine.** Journal of Pharmaceutical Sciences. 63(6):848-853, 1974.

A series of mono and di-N-substituted 2-(1-indanyl)-ethylamines was prepared and screened for monoamine oxidase inhibition and serotonin antagonism. Synthetic methods for their preparation are described and the procedures used for their screening along with the activity found are discussed. Several test compounds gave evidence of monoamine oxidase inhibition in vitro and in vivo. Several compounds possess central myorelaxant and ataractic properties of the type exhibited by the minor tranquilizers. 18 references. (Author abstract modified)

185980 Parmar, Surendra S.; Joshi, P. C.; Ali, Basheer; Cornatzer, William E. Dept. of Biochemistry, Univ. of North Dakota School of Medicine, Grand Forks, ND 58201 **Anticonvulsant activity and inhibition of respiration in rat brain homogenates by substituted oxadiazoles.** Journal of Pharmaceutical Sciences. 63(6):872-875, 1974.

Several 2,5-disubstituted 1,3,4-oxadiazoles were synthesized, characterized and tested for their effectiveness in inhibiting the respiratory activity of rat brain homogenate. All substituted oxadiazoles and their precursors, thiosemicarbazides, were found to exhibit nicotinamide adenine dinucleotide (NAD) dependant oxidations of pyruvate and alpha-ketoglutarate as well as the NAD independent oxidation of succinate. Anticonvulsant activity, as exhibited by protection against pentylenetetrazol induced seizures, with substituted thiosemicarbazides and the corresponding cyclized oxadiazoles ranged from 30% to 90% at a dose of 100mg/kg. The degree of protection afforded by the compounds was unrelated to their ability to inhibit oxidation of pyruvate, alpha-ketoglutarate and succinate. 14 references. (Author abstract)

02 DRUG DEVELOPMENT (PRECLINICAL SCREENING)

182634 Ito, Ryuta; Henomatsu, Hiroshi; Shimura, Mitsunaga. Department of Pharmacology, School of Medicine, Toho University, Omori, Tokyo, Japan **Pharmacological differences between fluphenazine enanthate and its hydrochloride.** Journal of the Medical Society of Toho University (Tokyo). 20(1/2):30-37, 1973.

The central actions of fluphenazine enanthate (Fl-En) were compared with those of fluphenazine hydrochloride (Fl-HCl) on onset and duration of actions. In rats, the inhibitory action of Fl-En on spontaneous EEG and responses to sensory stimulation reached the maximum 6 hours after the intraperitoneal injection, and continued for 24 hours, whereas the onset of Fl-HCl appeared over 2.0mg/kg and 10 to 15 minutes. The suppression of spontaneous motility in mice was observed over 6mg/kg, of Fl-En, 80 minutes after the injection but 10% of the active motility still remained. The sleeping time became longer according to dosage increase and this tendency was more evident in Fl-HCl. After 24 hours, the potentiation with Fl-HCl disappeared. The inhibitory action of Fl-En against apomorphine induced vomiting continued for 96 hours. Above data show that Fl-En possesses far milder and longer action than Fl-HCl. 11 references. (Author abstract modified)

182637 Yamauchi, Yoichi; Nakamura, Masaki; Koketsu, Kyozo. Tokyo Research Laboratories, Kowa Company, Ltd., Tokyo, Japan **Effects of alkali metals on spontaneous motor activities of mice.** Kurume Medical Journal (Kurume). 19(3):175-178, 1972.

The effects of alkali metals on spontaneous motor activities of mice were tested by the photocell counter method. Activity was depressed by a chronic administration of lithium and was accelerated by a chronic administration of rubidium or cesium. These effects of lithium and rubidium are in accord with the therapeutic effects of these metals on manic and depressive psychoses. Findings suggest the clinical utility of rubidium as an antidepressant agent in man. 18 references. (Author abstract modified)

182828 Chandra, Satish; Dandiya, P. C. Department of Pharmacology, S. M. S. Medical College, Jaipur, India **Central nervous depressant XV: synthesis and pharmacological screening of some trimethoxy azlactones.** Indian Journal of Hospital Pharmacy (New Delhi). 7(4):151-153, 1970.

In a search for a potent central nervous system depressant drug, three azlactone derivatives possessing a trimethoxy benzene were synthesized and their structures were confirmed by infrared spectra. Pharmacological screening revealed that these potentiated pentobarbital hypnosis in mice, caused a slight reduction in spontaneous motor activity in mice, and conditioned avoidance response in trained rats. They also caused a mild and transient hypotensive effect in anesthetized dogs. Only one of these compounds (d-benzoylamino-2,3,4-trimethoxy cinnamic acid) produced a mild hypothermic effect. 17 references. (Author abstract modified)

183598 Parmar, Surendra S.; Chaturvedi, A. K.; Chaudhary, A.; Brumleve, Stanley J. Department of Physiology and Pharmacology, School of Medicine, University of North Dakota, Grand Forks, ND 58201 **Substituted piperazinoquinazolones: relationship between selective inhibition of nicotinamide adenine dinucleotide-dependent oxidations and anticonvulsant activity.** Journal of Pharmaceutical Sciences. 63(3):356-360, 1974.

Several substituted piperazinoquinazolones were synthesized, characterized, and tested for their ability to affect the respiratory activity of rat brain homogenate. All piperazinoquinazolones were found to inhibit selectively nicotinamide adenine dinucleotide (NAD) dependent ozidations of pyruvate, citrate, DL-isocitrate beta-hydroxybutyrate, alpha-ketroglutarate, and NADH while the NAD independent oxidation of succinate remained unaltered. Inhibition of the oxidation of pyrovic acid by piperazinoquinazolones was concentration dependent, but added NAD, while stimulating the respiratory activity of brain homogenate, reduced the inhibition produced by these compounds. Some of these piperazinoquinazolones possessed anitconvulsant activity; however, this activity was found to be unrelated to their ability to inhibit the respiratory activity of the rat brain homogenate. 15 references. (Author abstract)

183599 De Leenheer, A. P. Faculteit van de Farmaceutische Wetenschappen, Bijksuniversiteit Gent, 135-De Pintelann, 9000-Gent, Belgium **Identification and quantitative determination of phenothiazine drugs in urine samples of psychiatric patients.** Ph Journal of Pharmaceutical Sciences. 63(3):389-394, 1974.

A gar - liquid chromatographic (GLC) method for the specific identification and quantitation of phenothiazine drugs excreted in urine at the microgram level is described. The phenothiazine drugs and less polar metabolites are isolated by two phase extraction with ether as an organic extractant. Quantitative determination at the microgram level is done on an acetylated fraction of the alcoholic extract by GLC using a suitable internal standard. The compounds are also identified by examining an aliquot of the final alcoholic extract by thin layer chromatography for supporting evidence of the GLC method's specificity. 2 references. (Author abstract)

184581 Hansl, N. R. Creighton University, Omaha, NB 68178 **A novel spasmolytic and CNS active agent: 3-(2-benzyl-methylamino ethyl) benzoic acid methyl ester hydrochloride.** Experientia (Basel). 30(3):271-272, 1974.

A novel spasmolytic and CNS active agent, 3-(2-benzyl-methylamino ethyl) benzoic acid methyl ester hydrochloride was synthesized. Subjects tested were a dog, rats, mice, and humans. Drug effect on retention was determined in drug and nondrug states of escape responses in rats. Improvements were noted in learning, short-term recall, long-term recall and correlation in man. Reports of the chemistry and pharmacology of the agent will be presented in the near future. 4 references.

03 MECHANISM OF ACTION: PHYSIOLOGICAL, BIOCHEMICAL AND PHARMACOLOGICAL

182212 Canfield, Don R.; Antelman, Seymour M; Lippa, Arnold S.; Fisher, Alan E. University of Pittsburgh, Pittsburgh, PA 15213 **Amphetamine-induced alteration of biogenic amines and self-stimulation.** Federation Proceedings. 32(3):754, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, amphetamine induced alteration of biogenic amines and self-stimulation were reported. Rats implanted with hypothalamic electrodes and trained to self-stimulate were treated with d-amphetamine sulfate alone or in combination with FLA-63 (bis(4-methyl-l-homopiperazinylthiocarbonyl)- disulfide, 25mg/kg ip), which produces up to 70% depletions of norepinephrine (NE) without affecting dopamine (DA). They were also tested with FLA-63 alone. In a 30 min self-stimulation test amphetamine alone or in combination with FLA-63 caused the same increase in self-stimulation, while FLA-63 alone had no effect. These data deemphasize the role of NE in self-stimulation and further implicate a possible involvement of DA in this phenomenon. (Author abstract modified)

182213 Zigmond, M. J.; Stricker, E. M. Psychobiology Program, University of Pittsburgh, Pittsburgh, PA 15213 **Recovery of feeding after 6-hydroxydopamine (6-HDA) or lateral hypothalamic lesions: The role of catecholamines.** Federation Proceedings. 32(3):754, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the role of catecholamines in the recovery of feeding after 6-hydroxydopamine (6-HDA) or lateral hypothalamic lesions was reported. Both the electrolytic and the biochemical lesioning procedures produce a variable depletion of telencephalic norepinephrine (NE) but an almost total depletion of striatal dopamine (DA), suggesting a role of this monoamine in the control of feeding. However, although the DA depletion is permanent, rats given either of the above treatments often recover from feeding deficits. In rats recovered from aphagia produced by 6-HDA or LH lesions, food intake is severely depressed by doses of alpha-methyltyrosine (AMT) which have no effect on control animals. Rats recovered from aphagia produced by 6-HDA again become aphagic after a third injection of 6-HDA and do not recover spontaneous ingestion. Recovery of feeding after 6-HDA or LH lesions may depend upon the functions of a small number of residual DA containing neurons. (Author abstract modified)

182214 Woodward, J. K.; Lucas, R. W. Merrell-National Laboratories, Division of Richardson-Merrell, Inc., Cincinnati, OH 45215 **Differential circulatory effects of various anorexigenic drugs.** Federation Proceedings. 32(3):754, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the differential circulatory effects of various anorexigenic drugs were reported. The acute differential circulatory effects of amphetamine (1), methamphetamine (2), phenmetrazine (3), chlorphentermine (4), fenfluramine (5), aminorex (6) and diethylpropion (7) on pulmonary and aortic blood pressures were examined. Results showed that 1, 2, and 3 did not produce a differential pressor response, whereas the pressor effects of 4, 5, and 6 were chiefly on the pulmonary circulation. Diethylpropion, on the other hand, had little or no effect on either system. Indeed, occasionally a fall in pulmonary pressure was elicited. Evaluation of these results show: 1) a striking similarity of fenfluramine to aminorex and less so to chlorphentermine; 2) a close quantitative relationship of d-amphetamine to methamphetamine and qualitatively to phenmetrazine. Diethylpropion resembled none of these drugs since it appeared to be essentially devoid of significant pressor activity. (Author abstract modified)

182216 Leibowitz, Sarah F. Rockefeller University, New York, NY 10021 **Alpha-adrenergic receptors mediate suppression of drinking induced by hypothalamic amphetamine injection.** Federation Proceedings 32(3):754, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, a study of the suppression of drinking induced by hypothalamic amphetamine (AMPH) injection by alpha-adrenergic receptors was reported. Experiments with adrenergic antagonists show that AMPH induced suppression of drinking can be reliably reduced by phentolamine, an alpha-receptor blocker, but is unaffected by propranolol, a beta-receptor blocker. This finding suggests that the suppression of water intake induced by hypothalamic injection of AMPH is mediated by alpha-adrenergic receptors located presumably in the hypothalamus. Since perifornical hypothalamic injection of norepinephrine also produces an alpha-adrenergic suppression of drinking effect it is possible that the effect of AMPH on water intake is mediated by endogenous norepinephrine. (Author abstract modified)

182218 Manno, Joseph E.; Manno, Barbara R. Department of Pharmacology, LSU Medical Center, Shreveport, LA 71130 **The interaction of delta9-tetrahydrocannabinol (THC), pentobarbital and SKF-525A with the cardiovascular system of the rat.** Federation Proceedings. 32(3):755, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the interaction of delta9-tetrahydrocannabinol (THC), pentobarbital and SKF-525A with the cardiovascular system of the rat were reported. A maximal bradycardia was produced in all conditions at 10 minutes after THC administration. The bradycardia reverted to a tachycardia at 60 minutes in unanesthetized rats. The initial bradycardia was greater in anesthetized animals than in unanesthetized rats. Pretreatment with SKF-525A potentiated the initial negative chronotropic action of THC, particularly in unanesthetized rats. The tachycardia at 60 minutes was also potentiated by SKF-525A. The implications of the pretreatment of SKF-525A were discussed with reference to alterations in THC and 11-hydroxy THC concentrations. (Author abstract modified)

182219 Barnard, M. Department of Pharmacology, University of Pittsburgh, Pittsburgh, PA 15213 **Mechanism of the negative chronotropic and inotropic effects of delta1-tetrahydrocannabinol (delta1-THC or delta9-THC).** Federation Proceedings. 32(3):755, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the mechanism of the negative chronotropic and inotropic effects of delta1-tetrahydrocannabinol (delta1 or delta9-THC) was examined. Intravenous administration of delta1-THC produced bradycardia and hypotension. The negative chronotropic action of delta1-THC was partially abolished after vagotomy. In isolated rabbit hearts, the effect of albumin with and without delta1-THC was examined. In all doses delta1-THC decreased ventricular pulse pressure (VPP) with only slight change in heartrate. Percent recovery of VPP was less with the higher dose; however, with the lower doses recovery was complete or near complete. Ethanol and albumin, the vehicles, did not have appreciable effects. It is postulated that delta1-THC decreases

heartrate primarily by influencing nerve activity and decreases myocardial force by direct and possibly indirect actions. (Author abstract modified)

182220 Haavik, C. O.; Hardman, H. F. Medical College of Wisconsin, Milwaukee, WI 53233 **Hypothermic action of delta9-tetrahydrocannabinol, 11-OH-delta9-tetrahydrocannabinol and 11-OH-delta8-tetrahydrocannabinol (delta9-THC, 11-OH-delta9-THC and 11-OH-delta8-THC) in mice.** Federation Proceedings. 32(3):755, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the hypothermic actions of delta9-tetrahydrocannabinol (delta9-THC), 11-OH-delta9-THC and 11-OH-delta8-THC in mice were reported. Delta9-THC and 11-OH-delta9-THC both lower body temperature immediately. Magnitude and duration of the hypothermic response are dose related. At low dose levels delta9-THC and 11-OH-delta9-THC do not differ significantly in onset, magnitude and duration of hypothermic action. 11-OH-delta8-THC also lowers body temperature significantly within 30 seconds after administration, but is less potent than is 11-OH-delta9-THC and has a shorter duration of action. The rapid onset of hypothermia following iv administration of delta9-THC suggests that this drug possesses intrinsic activity. A quantitative comparison of delta9-THC and 11-OH-delta9-THC indicates that both substances have similar hypothermic efficacy. (Author abstract modified)

182221 Kosersky, D. S. University of North Carolina, Chapel Hill, NC 27514 **Antipyretic, analgesic and antiinflammatory activity of delta9-tetrahydrocannabinol in the rat.** Federation Proceedings. 32(3):756, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the antipyretic, analgesic, and antiinflammatory activity of delta9-tetrahydrocannabinol (THC) as compared to phenylbutazone in the rat were examined. Dose related hypothermic responses were produced by THC in normal animals. THC significantly reduced elevated temperatures in yeast induced pyretic rats to near normal levels at doses which exhibited no hypothermic activity in normal rats. THC administered orally was essentially inactive at dose levels below those producing pronounced central nervous system depression. The oral antiinflammatory efficacy of delta9-THC was compared to phenylbutazone and acetylsalicylic acid. THC was ineffective in inhibiting carrageenin induced edema of the rat paw following acute or chronic administration. (Author abstract modified)

182222 Shih, T. M.; Oskoui, M. Department of Pharmacology, University of Pittsburgh, Pittsburgh, PA 15213 **The effects of delta1-tetrahydrocannabinol (delta1-THC or delta9-THC) and ethanol on monosynaptic and polysynaptic transmission in the central nervous system.** Federation Proceedings. 32(3):756, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the effects of delta1-tetrahydrocannabinol (THC) on monosynaptic (MS) and polysynaptic (PS) potentials (P), posttetanic potentiation (PTP), heartrate (HR), and blood pressure (BP) studied in anesthetized spinal cats were reported. Administration of THC effectively resulted in bradycardia, hypotension and depression of MSP in all experiments. No marked change occurred in the areas under the PSP. No direct relationship between the change in blood pressure and the observed changes in MS responses could be established. The percentage increased in MSP following tetanus was greater after THC; however, the absolute PTP value was less than the control PTP. It is concluded that THC depresses spinal MS activity, and that this alteration occurs independently of changes in blood pressure. (Author abstract modified)

182223 Perez-Reyes, Mario; Timmons, Martha C.; Lipton, Morris A.; Christensen, H. Dix.; Davis, Kenneth H.; Wall, Monroe E. Department of Psychiatry, University of North Carolina, Chapel Hill, NC 27514 **A comparison of the pharmacological activity of delta9-tetrahydrocannabinol and its monohydroxylated metabolites in man.** Federation Proceedings. 32(3):756, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the pharmacological activity of delta9-tetrahydrocannabinol (THC) and its monohydroxylated metabolites in man were compared. The degree of potency of THC metabolites in eliciting a marihuana like high in man was examined. Compounds were infused to normal, paid male volunteers human serum albumin as the vehicle of administration was used. It has been found that hydroxylation at the 11-position does not change potency, and at the 8beta position reduces it, and at the 8gamma position abolishes it. (Author abstract modified)

182224 Wajda, I. J.; Manigault, I.; Hudick, J. P.; Lajtha, A. New York State Research Institute for Neurochemistry and Drug Addiction, Ward's Island, New York, NY 10035 **Regional and subcellular distribution of choline acetyltransferase in the brain of normal and morphine treated rats.** Federation Proceedings. 32(3):757, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the regional and subcellular distribution of choline acetyltransferase in the brain of normal and morphine treated rats were examined. Homogenates from the caudate nucleus (CN), cerebral cortex (Cx) and hypothalamus (H) were fractionated, and the distribution of choline acetyltransferase (ChAc) was compared to that of protein, monoamine oxidase (MAO) and potassium. Synaptosomal and mitochondrial fractions were obtained from discontinuous Ficoll or sucrose gradients. Differences in the distribution of ChAc in the three brain regions were found and confirmed by use of continuous sucrose gradients. ChAc was localized in denser particles from CN than from Cx or H. The density of MAO containing particles, however, was similar from all three brain regions. K+ rich particles coincided with those containing ChAc in Cx and H, but were located in less dense fractions in CN. Morphine treatment did not influence the distribution of ChAc, but a slight shift of MAO toward lower density fractions was noticed in preparations from CN. Regional differences in the density of cholinergic particles parallel those found in uptake experiments. (Author abstract modified)

182225 Peterson, George R.; Shuster, Louis. Tufts University School of Medicine, Boston, MA 02111 **Effects of narcotic analgesics on enzymes of acetylcholine metabolism in cultured chick brain cells.** Federation Proceedings. 32(3):757, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the effects of narcotic analgesics on enzymes of acetylcholine metabolism in cultured chick brain cells were reported. Surface cultures of cells mechanically dissociated from the brains of 7 day chick embryos contain both neurons and flat cells. These cell types can be separated physically and assayed independently. The neurons contain choline acetyltransferase (ChAc) and acetylcholinesterase (AChEs), while the flat cells contain bu-

tyrylcholinesterase and carnitine acetyltransferase. Morphine sulfate (MSO4), added to the cultures, increased the activity of the neuronal enzymes by 50% in 24 hrs, but had no effect on the activity of enzymes in flat cells. The action of MSO4 could be blocked by the simultaneous addition of naloxone. Similar increases in the activity of ChAc and AChEs were observed in the brains of chick embryos treated with levorphanol in vivo. This observation suggests the development of tolerance to MSO4. There was no evidence for physical dependence when MSO4 was withdrawn from cultured cells. (Author abstract modified)

182226 Cheney, D. L.; Hanin, I. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Effect of acute and chronic morphine on specific radioactivities of choline and acetylcholine in mouse brain.** Federation Proceedings. 32(3):757, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the effects of acute and chronic morphine on specific radioactivities (S.A.)of choline (C) and acetylcholine (ACh) in mouse brain were reported. Mice were injected with phosphoryl (Me-14C) choline and killed at various times during 10 minutes following injection of the label. During these 10 minutes the concentrations of both Ch and ACh after A.M. were elevated to a new steady state, 20% higher than normal. However, the steady state of Ch and ACh was not altered after chronic morphine (C.M.). The relationship between the changes with time of Ch and ACh S.A. was different in acute morphine (A.M.)and saline treated mice. In A.M. the two S.A.'s did not diverge as in saline treated mice after the crossover point. After C.M. treatment both ACh and Ch S.A. were significantly increased compared with sham implanted mice. In this case, however, the relationship between the changes with time of Ch and ACh S.A. was not different in C.M. and saline treated mice. These data suggest different changes in the dynamics of cholinergic neurons elicited by A.M. and C.M.,respectively. (Author abstract modified)

182227 Domino, Edward F.; Matthews, John D.; Labrecque, Gaston. University of Michigan, Ann Arbor, MI 48104 **Effects of morphine, nalorphine and naloxone on rat brain release of acetylcholine.** Federation Proceedings. 32(3):757, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the effects of morphine, nalorphine and naloxone on rat brain release of acetylcholine (ACh) were reported. The effects of morphine, nalorphine, and naloxone were studied on neocortical release of ACh in midpontine pretrigeminal transected rats. Adult male rats were anesthetized with diethyl ether air for all surgery. A midpontine pretrigeminal transection was performed and anesthesia stopped. One hour later Ach was collected from a cup placed over the neocortex and bioassayed by using the dorsal muscle of the leech. Morphine and, to a lesser extent, nalorphine decreased ACh release. Naloxone was ineffective alone, but antagonized the action of morphine. The ACh antirelease effect of nalorphine was transient with recovery in 30 min. This explains the failure to show that nalorphine has an agonistic effect on brain ACh depletion in the rat. (Author abstract modified)

182228 Johnson, J. C.; Clouet, D. H. NYS Narcotic Addiction Control Commission Testing and Research Laboratory, Brooklyn, NY 11217 **Studies on the effect of acute and chronic morphine treatment on catecholamine levels and turnover in discrete brain areas of rats.** Federation Proceedings. 32(3):757, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, studies on the effect of acute and chronic morphine (M) treatment on catecholamine levels and turnover in discrete brain areas of rats were reported. With acute M treatment norepinephrine (NE) levels decreased at 30 min and returned to normal or above normal values by 60 min in all brain areas, while dopamine (DA) was decreased at 30 min and normal at 60 min. With chronic treatment NE levels remained decreased while DA levels were elevated. Tyrosine (T) levels and T specific activity were found not to change significantly with acute or chronic M treatment. NE synthesis was decreased by acute M treatment. (Author abstract modified)

182229 Santos, Carroll A., III ;Middaugh, Lawrence; Buckholtz, Neil; Zemp, John W. Medical University of South Carolina, Charleston, SC 29401 **Effects of methadone on activity and on brain monoamines in two mouse strains.** Federation Proceedings. 32(3):758, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the effects of methadone on activity and on brain monoamines in two mouse strains were reported. For the DBA strain, the initial injection of methadone produced an attenuation of locomotor activity associated with a cataleptic response. With continued administration, activity increased until it was equal to that of controls. For the C57 strain, the activity pattern across days was similar to that of the DBA strain but at a much higher level and without the initial depression. The results of the behavioral tests demonstrate that the reaction to methadone changes with increasing time on the drug and that the reaction obtained is strain dependent. In biochemical studies it was shown that norepinephrine (NE) levels were elevated in brains of DBA mice but not C57 mice chronically exposed to methadone. The biochemical results are not inconsistent with behavioral alterations. (Author abstract modified)

182230 Puri, Surendra K.; Lal, Harbans. Department of Pharmacology & Toxicology, College of Pharmacy, University of Rhode Island, Kingston, RI 02881 **Effect of morphine, haloperidol, apomorphine and benztropine on dopamine turnover in rat corpus striatum: evidence showing morphine-induced reduction in CNS dopaminergic activity.** Federation Proceedings. 32(3):758, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, a study of morphine induced reduction in CNS dopaminergic activity by morphine, haloperidol, apomorphine and benztropine on dopamine turnover in rat corpus striatum was reported. Dopamine turnover was measured in rat corpus striatum as a decline in dopamine after inhibition of its synthesis by alpha methyl-p-tyrosine methyl ester. Pretreatment with morphine or haloperidol increased the turnover of dopamine in a dose dependent manner. Apomorphine or benztropine, on the other hand, caused a dose dependent decrease in dopamine turnover. There was an enhancement of dopamine turnover when morphine was administered to the rats pretreated with a small dose of haloperidol but not with a large dose of haloperidol. Apomorphine or benztropine reversed the effect of morphine or haloperidol. The neurochemical data suggest that, like haloperidol, acute morphine administration reduced dopaminergic transmission in the CNS. (Author abstract modified)

182231 Ho, I. K.; Loh, H. H.; Way, E. Leong. University of California, San Francisco, CA 94122 **Effect of gamma-aminobu-**

tyric acid (GABA) on morphine analgesia, tolerance and physical dependence. Federation Proceedings. 32(3):758, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the effect of gamma-aminobutyric acid (GABA) on morphine analgesia, tolerance and physical dependence in mice was reported. Significant antagonism of morphine analgesia was present as evidenced by an increase in morphine AD50 in both nontolerant mice and in mice rendered tolerant to morphine by pellet implantation for 3 days. When GABA or aminooxyacetic acid (AOAA) was administered before and during pellet implantation, the increase in the morphine AD50 was greater than that in mice receiving GABA or AOAA 3 days after pellet implantation. Thus, development of tolerance to morphine appeared to be enhanced. Pretreatment with the same drugs also appeared to enhance the development of physical dependence on morphine; measurement of dependence intensity by the naloxone precipitated abstinence test revealed that the amount of naloxone required to elicit stereotyped jumping was reduced. (Author abstract modified)

182232 Gerald, M. C.; Braytenbah, E. A.; Hsu, S. Y. Department of Pharmacy, Ohio State University, Columbus, OH 43210 **Effects of amphetamine isomers on neuromuscular transmission in rat phrenic-nerve diaphragm preparation.** Federation Proceedings. 32(3):772, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the effects of amphetamine isomers on neuromuscular transmission in rat phrenic nerve diaphragm preparation were reported. Both isomers produced initial stimulation followed by blockade with repeated additions of drug. With indirect stimulation, the blocking effects of D-AMP were observed after the 3rd dose with no stimulation. By contrast, L-AMP caused smaller initial stimulation and did not produce blockade until 25 min after the 5th dose. Cooling inhibited the AMP block. Physostigmine enhanced the rate of D- and L-AMP block, effects antagonized by cooling bath from 37 to 25 degrees. Curare antagonized D-AMP block in most experiments. After tetrodotoxin pretreatment, D-AMP completely and rapidly blocked direct nerve stimulation. Although most of the evidence suggests that the AMP isomers are depolarizing blockers, the temperature antagonized block is indicative of a competitive block. (Author abstract modified)

182234 Giachetti, A.; Hollenbeck, R. A.; Shore, P. A. University of Texas Southwestern Medical School, Dallas, TX 75235 **Evidence for persistent reserpine binding to amine storage vesicle membranes.** Federation Proceedings. 32(3):783, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, evidence for persistent reserpine (R) binding to amine storage vesicle membranes in rat adrenals was presented. R content was 1.2-1.7ng/gland pair. Of this, over 80% was in the granular fraction. After density gradient centrifugation of the resuspended granular fraction in sucrose, R and catecholamines (CA) were found together in a band near the bottom, while the bulk of protein and mitochondria (MAO activity) lay in a band of much lighter density. Membrane bound R did not exchange with fresh granules since incubation of R rich membranes with 26,000 x g granule fraction from untreated rats followed by gradient centrifugation of the mixture resulted in a separation of R from CA. The results indicate that R persisting 48-65 hrs after treatment is irreversibly bound to membranes of CA vesicles. (Author abstract modified)

182243 Buckley, Joseph P.; Jandhyala, Marie L.; Barry, Herbert, III; Manian, Albert A. Department of Pharmacology, University of Pittsburgh School of Pharmacy, Pittsburgh, PA 15213 **Pharmacology of mono and disubstituted chlorpromazine metabolites.** Federation Proceedings. 32(3):786, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, chlorpromazine (CPZ) and 10 of its mono and disubstituted metabolites were investigated for their effects on the central nervous system of male rats and mice. All of the compounds decreased motor activity and respiration, and all but two of the compounds decreased heartrate in rats. The most potent metabolite depressing spontaneous motor activity of mice was 3,7-dihydroxy-CPZ in comparison to CPZ. 7,8-Dihydroxy-CPZ did not alter forced motor activity, but did induce a dose related depression of spontaneous motor activity, and 7-hydroxy-8-methoxy-CPZ also produced a marked decrease in spontaneous motor activity with minimal effects on forced motor activity. None of the compounds demonstrated anticonvulsant activity and only 7-hydroxy-CPZ elicited effects suggesting possible antidepressant activity. Barbiturate sleeping time was potentiated by all of the compounds, mainly due to their CNS depressant properties. (Author abstract modified)

182244 Barofsky, I.; Williams, D. A.; Correia, J. Massachusetts College of Pharmacy, Boston, MA 02115 **Behavioral and physiological activity of deaminated metabolites of mescaline.** Federation Proceedings. 32(3):786, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the relative activity of mescaline, 3,4,5-trimethoxyphenylacetic acid (TMPA), 3, 4, 5-trimethoxyphenylethanol (TMPA) or 3, 4, 5-trimethoxyphenylacetaldehyde (TMPAld) were compared. Rats trained on a fixed-ratio (FR-50) schedule of food reinforcement showed a dose related decrease in performance following ip injections of mescaline. The effect of intracerebral injections of either 10 microliters of saline, 10 of mescaline or the bisulfite addition product of TMPAld on the body temperature of mice indicated that TNPAld had a hypothermic effect comparable to that of mescaline. The data were interpreted as providing support for the suggestion that the deaminated metabolites of mescaline were biologically active. (Author abstract modified)

182245 Huang, J. T. Texas Research Institute of Mental Science, Houston, TX 77025 **Amphetamine and pentobarbital effects on the discriminative response control by deprivation of rapid eye movement sleep (REMS).** Federation Proceedings. 32(3):786, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, amphetamine and pentobarbital effects on the discriminative response control by deprivation of rapid eye movement sleep (REMS) in rats were reported. Amphetamine given to rats that were deprived of REMS did not change the discriminative response, while this drug did significantly change the discriminative response in rats not deprived of REMS. Pentobarbital differed from amphetamine and did not change responding in rats not deprived of REMS while significantly changing responses in rats deprived of REMS. The results indicate that REMS deprivation can be a cue for discrimination learning; they also indicate that the stimulus properties of amphetamine are masked by the stimulus properties of REMS deprivation and stimulus properties of pentobarbital are masked by the stimulus properties of having REMS. (Author abstract modified)

182246 Lytle, Loy D.; McGuire, Robert A. MIT, Cambridge, MA 02139 **The ontogeny of amphetamine-induced alterations in thermal regulation.** Federation Proceedings. 32(3):786, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the ontogeny of amphetamine induced alterations in thermal regulation was discussed. Preweanling rats were exposed to ambient temperatures of 22 or 37 degrees C for 1 hr. Following this adapation period, they were injected with d-amphetamine sulfate or an equivalent volume of the saline. At the 22 degrees C ambient temperature, amphetamine produced a dose related hypothermia in 5-day-old rats; the drug induced hyperthermia was not observed until 15 days of age. In contrast, all age groups in the 37 degrees C ambient temperature condition showed marked, dose related increase in body temperature after the injection. The data with neonates suggest that thermic effects of amphetamines are present in animals normally lacking mechanisms for thermoregulation. (Author abstract modified)

182248 Sudilovsky, A.; Ellinwood, E. H. Duke University, Durham, NC 27710 **EEG changes & motor impairment after disulfiram administration to cats.** Federation Proceedings. 32(3):791, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, electroencephalographic changes and motor impairment after disulfiram administration to cats were reported. In the acute experiments, increased amplitude (but not frequency, duration or number of cycles) of spindle activity in the olfactory bulb, amygdala, and accumbens was noted. After repeated doses there was, in addition, an increase in slow waves and dysrhythmic activity. This was seen to progress, under auditory stimulation, from auditory cortex afterdischarges to electrographic seizure activity. All chronic animals showed loss of righting reflexes, muscle wasting and progressive ataxia. The early appearance of ascendent neuropathy impairs spontaneous activity in cats after repeated oral DS administration and suggests that sensitivity to it is higher in this than in other animal species. (Author abstract modified)

182249 Suria, Amin. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeth's Hospital, Washington, DC 20032 **Anticonvulsants and post tetanic potentiation.** Federation Proceedings. 32(3):792, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the effects of several classes of anticonvulsants on posttetanic potentiation (PTP) of excitatory postsynaptic potential (EPSP) recorded from the curarized sympathetic ganglia of bullfrog were reported. Anticonvulsant and sedative benzodiazepines such as diazepam and chlordiazepoxide significantly decreased the PTP of EPSP. Another benzodiazepine, Ro 5-5807, a nonsedative anticonvulsant, also produced an inhibitory effect on the PTP; methyldiazepam in the presence of subthreshold dose of diazepam suppressed PTP of EPSP. A prototype of another class of anticonvulsant drugs, diphenylhydantoin (nonsedative), inhibited PTP proportionally to the concentration. Phenobarbital and phenetharbital inhibited PTP, whereas hexobarbital was ineffective. Data suggest that a reduction of PTP may be elicited by agents that produce anticonvulsant action. In the various drugs tested sedative properties are unrelated to the inhibition of PTP of EPSP. (Author abstract modified)

182250 Schaeffer, J. C.; Nagami, G. T.; Butcher, S. UCLA School of Medicine, Los Angeles, CA 90024 **Inhibition of the synaptosomal uptake mechanisms for L-norepinephrine and dopamine by N-arylalkyl DL-amphetamine derivatives.** Federation Proceedings. 32(3):815, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the inhibition of the synaptosomal uptake mechanisms for L-norepinephrine and dopamine by N-arylalkyl DL-amphetamine derivatives was reported. A nonstriatal and a striatal rat brain preparation were employed as models of the l-norepinephrine and dopamine transport systems, respectively. The I50 values for d-amphetamine and the homologous series, N-benzyl, N-phenethyl, N-3-phenylpropyl, and N-4-phenylbutyl dl-amphetamine are given. The data indicate a large bulk tolerance region adjacent to the amine binding site in both carrier systems which is at least partially hydrophobic in nature. The N-benzyl and N-4-phenylbutyl derivatives show the most selectivity, favoring the norepinephrine mechanism by a factor of 10. (Author abstract modified)

182251 Vrbanac, J. J.; Tilson, H. A. Michigan State University, East Lansing, MI 48823 **Effect of d-amphetamine (d-A) and 2,5-dimethoxy-4-methylamphetamine (DOM) on the in vivo release of 14C-norepinephrine (NE) into the lateral ventricle of rats.** Federation Proceedings. 32(3):815, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the effects of d-amphetamine (d-A) and 2,5-dimethoxy-4-methylamphetamine (DOM) on the in vivo release of 14C-norepinephrine (NE) into the lateral ventricle of rats were reported. Both DOM and d-A produced increases in percentage of 14C-NE, with smaller increases in normetanephrine in samples following injection. Other rats that had been treated with 6-hydroxydopamine intraventricularly before implantation of the push pull cannula showed no increase in radioactivity in the perfusate following injections of d-A, DOM, or NaCl. The data suggest that d-A and DOM act in a similar manner to release and/or to block the reuptake of NE in catecholaminergic nerve terminals surrounding the cerebral lateral ventricular system of the rat. (Author abstract modified)

182254 Seifter, Joseph; Friedman, Eitan; Gershon, Samuel; Ventura, Daniel F.; Seifter, Eli. New York Medical College, Valhalla, NY 10595 **Effect of 2-arylalanines, 2-arylserines, tetraphenylboron and 1,2-dl(2,4-dichlorophenyl)-ethanolamine on levels of serotonin (5HT), norepinephrine (NE) and dopamine (DM) in whole brain of mice.** Federation Proceedings. 32(3):816, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the effects of 2-arylalanines, 2-arylserines, tetraphenylboron and 1,2-Dl(2,4-dichlorophenyl)-ethanolamine on levels of serotonin(5HT), norepinephrine(NE) and dopamine(DM) in whole brain of mice were reported. p-Fluorophenylserine, p-anisylserine and beta-naphthylserine did not alter levels of 5HT, NE or DM. The convulsant boron quaternary lowered 5HT level 47%, while the depressant ethanolamine derivative raised it 77%. p-Chlorophenylalanine, p-chlorophenylserine, piperonylserine and p-dimethylaminophenylserine lowered 5HT about 33% and o-chlorophenylalanine 25%. p-Nitrophenylserine lowered 5HT 38% but also raised DM 52%. o-Chlorophenylserine lowered both 5HT and NE. a-Naphthylserine and 3,4-dichlorophenylalanine lowered only NE. p-Tolylserine and 3,4,5-trimethoxyphenylserine increased DM 24% and 20%. (Author abstract modified)

182255 Day, R. P.; Smith, C. B. Department of Pharmacology, University of Michigan, Ann Arbor, MI 48104 **Effects of**

chronic administration of amphetamine upon the catecholamine content of mouse brain. Federation Proceedings. 32(3):816, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the effects of chronic administration of amphetamine (AM) upon the catecholamine content of mouse brain were reported. After 4 days of repeated AM administration, brain norepinephrine (NE) content was decreased by about 40%. With continued administration for 3 additional days brain NE content returned to control levels. Brain dopamine (DA) content was decreased at both 4 and 7 days. In specific areas of brain, after 7 days of repeated AM administration, the NE content of cerebral cortex and brainstem was decreased, but the NE content of diencephalon had returned to control levels. These results indicate that tolerance develops to the catecholamine depleting effects of AM in certain regions of the mouse brain. (Author abstract modified)

182256 Anagnoste, Berta; Shirron, Catherine; Goldstein, Menek. Department of Psychiatry, Neurochemistry Lab, NYU Medical Center, New York, NY 10016 **The effect of dopamine receptor stimulating agents and of N,O-dibutyryl-cyclic AMP on C14-dopamine synthesis in striatal slices of rats.** Federation Proceedings. 32(3):816, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the effects of drug induced stimulation or blockade of dopamine receptors on C14-dopamine synthesis from C14-tyrosine in striatal slices of rats were reported. The dopamine receptor stimulating agents apomorphine or Trivastal inhibit effectively the biosynthesis of C14-dopamine from C14-tyrosine in striatal slices even at micromolar levels. The blockade of dopamine receptors by treatment of rats with haloperidol results in an enhancement of C14-dopamine biosynthesis in striatal slices. Treatment of rats with haloperidol antagonizes the Trivastal induced inhibition of C14-dopamine synthesis. These findings suggest that a receptor mediated feedback mechanism is involved in the regulation of striatal dopamine synthesis. (Author abstract modified)

182344 Doteuchi, M.; Costa, E. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeth's Hospital, Washington, DC 20032 **Pentylenetetrazol convulsions and brain catecholamine turnover rate in rats and mice receiving diphenylhydantoin or benzodiazepines.** Neuropharamcology (Oxford). 12(11):1059-1072, 1973.

The effects of diphenylhydantoin and benzodiazepines on brain catecholamine turnover were studied in rats exposed to cold. Diphenylhydantoin decreased the turnover of catecholamines in cerebellum and other brain areas of rats exposed to cold but it did not antagonize the convulsions elicited by pentylenetetazol. Findings suggest the action of benzodiazepines on turnover of norepinephrine (NE) and striatal dopamine (DA) in reducing turnover rate cannot be related to a direct action on amine metabolism. A diazepam analogue, RO-5-58-07, reduces turnover rate of brain NE in mice but not in rats exposed to cold. This drug does not antagonize pentylenetetrazol convulsion in rats but is active in mice. 26 references. (Author abstract modified)

182345 Starke, K.; Montel, H. Pharmakologisches Institut, Klinikum der Universitat Esssen, D-4300 Essen, Germany **Involvement of alpha-receptors in clonidine-induced inhibition of transmitter release from central monoamine neurones.** Neuropharmacology (Oxford). 12(11):1073-1080, 1973.

Clonidine's effect on noradrenaline release from cerebral neurones was studied, and its action on the release of 5-hydroxytryptamine is described. Studies using slices of rat cerebral cortex indicate that clonidine decreases, and phentolamine and phenoxybenzamine increase, the stimulation induced release of noradrenaline from cerebral neurones by an activation and a blockade of alpha receptors, respectively. A variety of secretory cells (secreting catecholamines, acetylcholine, 5-hydroxytryptamine, insulin or renin) seem to be endowed with structures similar to alpha adrenergic receptors, which can modulate the secretion process. 32 references. (Author abstract modified)

182347 Lidbrink, P.; Farnebo, L.-0. Dept. of Histology, Karolinska Institutet, S-10401 Stockholm, Swden **Uptake and release of noradrenaline in rat cerebral cortex in vitro: no effect of benzodiazepines and barbiturates.** Neuropharmacology (Oxford). 12(11):1087-1095, 1973.

The effects of two barbiturates (phenobarbitone and pentobarbitone) and one benzodiazepine (chlordiazepoxide) were studied on uptake, retention and spontaneous and stimulation induced release of 3H-noradrenaline in rat cerebral cortex slices in vitro. The drugs, in a wide range of concentrations, did not interfere with the uptake and retention of 3H-noradrenaline nor did they change the spontaneous release when slices, preincubated with 3H-noradrenaline were rinsed together with the drug. The field stimulation induced release of 3H-noradrenaline was also unaffected by these drugs. Pentobarbitone did not affect the amphetamine induced release of 3H-noradrenaline from the slices. Findings suggest that it is improbable that a previously reported decrease in turnover of noradrenaline in the cerebral cortex as a result of barbiturates and benzodiazepines is mediated via a direct effect on the noradrenaline nerve terminals. 42 references. (Author abstract modified)

182348 Hunt, W. A. National Institute on Alcohol Abuse and Alcoholism, NIMH, St. Elizabeth's Hospital, Washington, DC 20032 **Changes in the neuro-excitability of alcohol-dependent rats undergoing withdrawal as measured by the pentylenetetrazole seizure threshold.** Neuropharmacology (Oxford). 12(11):1097-1102, 1973.

Changes in the excitability of the nervous system after the cessation of chronic alcohol treatment was investigated in rats by measuring the pentylenetetrazole (PTZ) seizure threshold. On the day of withdrawal, PTZ seizure thresholds were significantly reduced, while an elevation was observed from 1 day to 4 weeks after withdrawal. Multiple convulsions were noted after exposure to PTZ from 1 to 7 days after withdrawal. The elevation in PTZ threshold is apparently not related to physical dependence since administering alcohol once daily for 14 days resulted in no overt withdrawal syndrome but still led to a significant increase in the PTZ threshold. Possible acceleration in the rate of metabolism of PTZ as a result of chronic administration of alcohol does not appear to contribute significantly to the elevated PTZ thresholds. 18 references. (Author abstract modified)

182441 Eichelman, B. S., Jr. Stanford University Medical Center, Stanford, CA **Rubidium salts: basic mechanisms of action.** Psychopharmacology Bulletin. 10(1):27-32, 1974.

Basic mechanisms of action of rubidium salts were reported at a workshop entitled 'Rubidium: Safety and Potential as an Antidepressant,' which was held by the National Institute of Mental Health in November 1972. Presentations demonstrated that rubidium can alter animal behavior, central and peripheral

biogenic amine metabolism, and electrolyte balance. Questions raised by these effects are discussed. 23 references.

182547 Yasuhara, Motohiro; Naito, Hiroe. Kansai Medical School, Moriguchi, Osaka, Japan **Electrophysiological studies of the effects of CDP-choline on the central nervous system.** Journal of Kansai Medical School (Osaka). 23(1), Supplement:1-4, 1971.

Electrophysiological studies of the effects of cytidine diphosphate choline (CDP-choline) on the central nervous system of rabbits are reported. The agent exerted an accelerating effect on the arousal reaction, but inhibited the recruiting response in many of the animals. It was demonstrated that CDP-choline is an effective agent as a stimulant (a therapeutic agent for such cases as intoxication with hypnotics). To compare the effects of CDP-choline on the muscular discharges from forelimb and hindlimb with those of the arousal reaction, the effects on the muscular discharge from the forelimb tended to be paralleled by those on the arousal reaction, but those on the discharge from the hindlimb were not paralleled by those on the arousal reaction. From the results, it has been proved that this substance is an effective agent for the treatment of acute disturbance of consciousness due to cerebral injury and its sequela. 8 references.

182549 Kimishima, Kenjiro; Tanabe, Kyoko; Yamazaki, Michiyo; Oikawa, Toshihiko; Fujitani, Yoshiko; Ogura, Chikara. Department of Pharmacology, Tottori University School of Medicine, Japan **Central nervous action of flurazepam, a new benzodiazepine derivative.** Journal of the Yonago Medical Association (Yonago). 23(1):63-72, 1972.

The effects of flurazepam on the central nervous system were analyzed in mice, rats, rabbits and cats. Diazepam and nitrazepam were used as control materials. Following intraperitoneal administration of flurazepam in chronically implanted rabbits, electroencephalographic properties in spontaneous electroencephalograms such as slow waves with high amplitudes in the neocortex were observed, and the arousal responses by stimulation of the hypothalamus and midbrain reticular formation and the seizure discharges induced by stimulation of the amygdala were inhibited. On the sleep cycles of cats, flurazepam increased the duration of the behavioral arousal and of the waking states, and decreased the duration of slow and fast wave sleeps. Based on the results obtained, it was concluded that flurazepam is a sleep inducer -- a mild minor tranquilizer. 16 references. (Author abstract modified)

182555 Sawada, Hideo; Hara, Akira; Yano, Hiroko; Kido, Akira. Department of Legal Medicine, Gifu University School of Medicine, Gifu, Japan **Absorption, distribution, excretion and metabolism of bromazepam in rabbit.** ACTA Scholae Medicinalis Universitatis in Gifu (Gifu). 21(4):237-247, 1973.

The absorption, distribution, excretion and metabolism of bromazepam in rabbits was investigated. For the total excretion of bromazepam (BZ) +3-OH BZ, 2-amino-5-bromobenzoylpyridine (ABBP) and 3-OH ABBP in urine and feces of rabbits administered with BZ, 71.5% and 78.4% of the dose was excreted in 24 hours in the 20mg/kg administration cases and the 100mg/kg administration cases respectively. After the administration of BZ 20mg/kg or 100mg/kg, the blood level of rabbits reached the maximum in 1-4 hours, half-life in 6-7 hours, and almost vanished in 24 hours. After oral administration, BZ was absorbed rather rapidly. BZ was distributed relatively highly in the brain, liver, kidney and bile in the early period after administration, and low in the lung, spleen, and testis. After BZ was absorbed rather rapidly, a portion of the excreted BZ was hydrolyzed at 3-position of the skeleton of BZ into the glucuronide conjugates. From the results obtained, it seems that 3-OH ABBP was excreted as glucuronide conjugated compounds. 7 references. (Author abstract modified)

182715 Walsh, Carol T.; Levine, Ruth R. Dept. of Pharmacology and Experimental Therapeutics, Boston University Medical Center, 80 E. Concord St., Boston, MA 02118 **Drug absorption in rats pretreated with antibiotics.** Journal of Pharmacology and Experimental Therapeutics. 188(2):277-286, 1974.

The intestinal absorption of pharmacologic agents was studied in rats pretreated with antibiotics to determine the effects on the drug absorption rate by alterations in the bacterial population in the intestinal tract produced by the antibiotics. The antibiotics used were neomycin, penicillin, lincomycin, and tetracycline. The absorption rates of diphenylhydantoin, tetracycline, benzomethamine, and chlorpromazine were determined. The results suggest that the changes observed in the indigenous flora of the rat do not significantly affect the factors that are critical to the normal absorption process of pharmacologic agents, since the alterations in the bacterial population of the ileum induced by antibiotic regimens produced no measurable changes in the in vivo absorption of a series of drugs. 46 references. (Author abstract modified)

182716 Dyer, Donald C. Department of Pharmacology, School of Medicine, University of Washington, Seattle, WA 98195 **Evidence for the action of d-lysergic acid diethylamide, mescaline and bufotenine on 5-hydroxytryptamine receptors in umbilical vasculature.** Journal of Pharmacology and Experimental Therapeutics. 188(2):336-341, 1974.

The results of a study of the mechanism by which hallucinogens contract umbilical vasculature, which support the hypothesis that contraction by d-lysergic acid diethylamide (LSD), mescaline, and bufotenine is mediated via 5-hydroxytryptamine (5-HT), are presented. The classical protection type experiment described by Furchgott was used. Mescaline, bufotenine, and 5-HT clearly protected 5-HT receptors while 5-HT protected bufotenine, mescaline, and LSD receptors. In addition, mescaline protected LSD receptors. Also, 5-HT does not protect norepinephrine (NE) or acetylcholine receptors, yet NE and acetylcholine can protect their own receptors under appropriate conditions. The fact that phenoxybenzamine did not block contractions to angiotensin supports the idea that the protection observed was not on the contractile apparatus itself but rather on specific receptors. 11 references. (Author abstract modified)

182717 Iwasawa, Y.; Gillis, C. N. Biological Research Laboratory, Tanabe Seiyaku Co., Ltd. Toda, Saitama, Japan **Pharmacological analysis of norepinephrine and 5-hydroxytryptamine removal from the pulmonary circulation: differentiation of uptake sites for each amine.** Journal of Pharmacology and Experimental Therapeutics. 188(2):386-393, 1974.

The effect of drugs known to influence extraneuronal amine uptake in other tissues was studied on the lung removal of norepinephrine (NE) and 5-hydroxytryptamine (5-HT). Removal of either NE or 5-HT, each at a concentration of 1.5micromolar, from the vascular space of rabbit lung perfused in vitro was significantly reduced by cocaine, phenoxybenzamine, imipramine, and, to a lesser degree, by normetanephrine. Aminophylline or phentolamine reduced removal of only NE, while propranolol was ineffective as an

inhibitor. The observation that, although uptake of amines was unaffected, vasconstriction in response to infusion of NE and particularly 5-HT was elevated significantly by 6-hydroxydopamine pretreatment supports the proposal that pulmonary vascular response is functionally unrelated to amine uptake by the lung. 20 references. (Author abstract modified)

182718 Sampath, S. S.; Neff, N. H. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **The elimination of 5-hydroxyindoleacetic acid from cerebrospinal fluid: characteristics of the acid transport system of the choroid plexus.** Journal of Pharmacology and Experimental Therapeutics. 188(2):410-414, 1974.

Some of the characteristics of the acid transport system of the choroid plexus that are responsible for eliminating 5-hydroxyindoleacetic acid (5-HIAA) from the cerebrospinal fluid (CSF) and an evaluation of the effects of drugs and some of the metabolites of the biogenic amines on the transport system are presented. The isolated choroid plexus is capable of concentrating 5-HIAA against a gradient and the uptake mechanism obeys Michaelis-Menten kinetics. Substances that are normally found in CSF, such as homovanillic acid, 3-methoxy-4-hydroxyphenylethyleneglycol sulfate, and cyclic 3'5'-adenosine monophosphate, all of which are thought to be cleared from brain by an anionic transport system, were not potent uptake blocking drugs. In contrast, probenecid, cephaloridine, and indoleacetic acid blocked the uptake of 5-HIAA. Furthermore, it appears that there may be transport systems in the brain located at sites other than the choroid plexuses. 20 references. (Author abstract modified)

182720 Oesch, Franz. Biozentrum of the University of Basel, Klingelbergstrasse 70, CH-4056 Basel, Switzerland **Transsynaptic induction of choline acetyltransferase in the preganglionic neuron of the peripheral sympathetic nervous system.** Journal of Pharmacology and Experimental Therapeutics. 188(2):439-446, 1974.

Treatment of rats with reserpine, which produces a transsynaptic induction of tyrosine hydroxylase and dopamine-beta-hydroxylase in the terminal adrenergic neuron, which also leads to an enhanced synthesis of choline acetyltransferase in the preganglionic cholinergic neuron is examined. The results demonstrate a marked increase in rat choline acetyltransferase activity of superior cervical and stellate ganglia and of the adrenal gland after the administration of reserpine. Evidence is provided that, in the adrenal gland, as well as in the superior cervical ganglion, choline acetyltransferase activity is localized exclusively in the preganglionic nerve terminals. 36 references. (Author abstract modified)

182721 Baumel, Irwin P.; Pitterman, Arthur; Patel, Girish; DeFeo, John J.; Lal, Harbans. Department of Pharmacology, Schools of Medicine and Dentistry, Georgetown University, Washington, DC 20007 **Mechanisms underlying potentiation of barbiturate action by sodium nitrite in the mouse: the role of methemoglobin-induced hypoxia.** Journal of Pharmacology and Experimental Therapeutics. 188(2):481-489, 1974.

The role of methemoglobin induced hypoxia in the interaction of nitrate containing compounds with various classes of centrally active drugs, which suggests that sodium nitrate treatment can enhance barbiturate action both by decelerating hepatic detoxification and by altering central nervous system sensitivity, is discussed. The barbiturates were chosen as prototypes since their metabolic disposition and pharmacologic activity are well documented. Sodium nitrate was used as it produces a sustained methemoglobinemia in the mouse without prior conversion to an active metabolite. The primary mechanisms underlying the alterations in barbiturate action induced by sodium nitrate appear to be the result of a tissue hypoxia produced as a result of methemoglobin formation. 35 references. (Author abstract modified)

182723 Heikkila, Richard E.; Cohen, Gerald. Dept. of Neurology, Mount Sinai School of Medicine, Fifth Avenue at 100th Street, New York, NY 10029 **The inhibition of (3H) biogenic amine accumulation into rat brain tissue slices by various tryptamine derivatives.** Research Communications in Chemical Pathology and Pharmacology. 7(3):539-547, 1974.

The inhibition of the accumulation of the (3H) biogenic amines (3H)dopamine and (3H)5-hydroxytryptamine in rat brain tissue by various nonhydroxylated, monohydroxylated, and dihydroxylated tryptamine derivatives is presented. Data were calculated and expressed as ED50 values, the concentrations at which the compounds caused a 50% inhibition of accumulation. 5-Hydroxytryptamine, 7-hydroxytryptamine, 5,6-dihydroxytryptamine, 3-(beta-aminoethyl)-5-hydroxybenzo(b)thiophene, tryptamine, and 6-hydroxytryptamine all inhibited (3H)serotonin accumulation. Dopamine, norepinephrine, and the catecholamine derivative 6,7-dihyroxytetrahydroisoquinoline were comparatively weak inhibitors of (3H)serotonin accumulation. The tryptamine derivatives 7-hydroxytryptamine, tryptamine, 3-(beta-aminoethyl)-5-hydroxybenzo(b)thiophene and 5-hydroxytryptamine were quite potent inhibitors of (3H)dopamine accumulation. 15 references. (Author abstract modified)

182725 Coscina, D. V.; Warsh, J. J.; Godse, D. D.; Stancer, H. C. Section of Neurochemistry, Clarke Institute of Psychiatry, 250 College St., Toronto, Ontario, M5T 1R8 Canada **Non-specificity of 5-hydroxytryptophan in repleting brain serotonin in rats with MFB lesions.** Research Communications in Chemical Pathology and Pharmacology. 7(3):617-620, 1974.

The synthetic capacity of brain parenchyma in medial forebrain bundle (MFB) lesioned rats was estimated using the peripheral decarboxylase inhibitor L-alpha-hydrazino-alpha-methyldopa (MK-486) in conjunction with a dose of 5-hydroxytryptophan (5-HTP) to normalize brain serotonin (5-HT) levels after such injury, is presented. While MK-486 plus 5-HTP produced larger 5-HT increments than saline plus 5-HTP in comparable hemispheres, the latter treatment produced greater percentage increases above endogenous 5-HT levels in lesioned versus nonlesioned hemispheres. This difference was not due to lesion induced damage to the blood-brain barrier. In the absence of MK-486, the proportionately greater 5-HT increments observed were felt to reflect contamination from 5-HTP utilization in brain capillary walls. 6 references. (Author abstract modified)

182727 Parmar, Surendra S.; Ali, Basheer; Spencer, Henry W.; Auyong, Theodore K. Department of Physiology, University of North Dakota School of Medicine, Grand Forks, ND 58201 **Induction of hepatic drug metabolizing enzymes by lithium treatment.** Research Communications in Chemical Pathology and Pharmacology. 7(3):633-636, 1974.

The effect of lithium pretreatment on aromatic hydroxylation, O-dealkylation, and N-dealkylation was investigated on the activity of rat liver drug metabolizing enzymes (DME). Administration of lithium carbonate at a dose of 50mg/kg every 12 hours for 21 days was found to increase the activity of DME to hydroxylate aniline by 30.9% and to undertake O-dealkylation of p-nitroanisole by 26.9%. Selective induction of

DME was observed during N-dealkylation of amidopyrine and cocaine where percent increase in DME activity was found to be 54.3% and 36.4% respectively while only 9.4% increase was observed with morphine. 10 references. (Author abstract modified)

182872 Saito, Hideya; Otani, Toru; Yomaida, Itaru; Bando, Mitsue; Tanabe, Tsuneyoshi. Department of Pharmacology, Hokkaido University School of Medicine, Sapporo, Japan **The influence of chronic administration of lithium carbonate on the brain norepinephrine content in rats.** Hokkaido Journal of Medical Science (Sapporo). 48(6):534-536, 1973.

Changes in catecholamine content of brain following long-term continuous administration of lithium carbonate were investigated in rats. No significant difference was detected between lithium treated groups and control groups treated only with saline. 8 references.

183228 Hattori, T.; Jakubovic, A.; McGeer, P. L. Department of Psychiatry, Faculty of Medicine, University of British Columbia, Vancouver 8, B.C., Canada **The effect of cannabinoids on the number of nuclear membrane-attached ribosomes in infant rat brain.** Neuropharmacology (Oxford). 12(10):995-999, 1973.

The pharmacologically active cannabinoids delta9-THC, delta8-THC, and 11-OH-delta9-THC were tested for effect on the number of nuclear membrane attached ribosomes in infant rat brains. Each compound caused a highly significant reduction in the ribosomes. The pharmacologically inactive agents cannabinol and cannabidiol had only a slight effect, while cannabigerol had a moderate effect. The activity was measured 3 hr after a 10mg/kg s.c. dose. The duration of effect was tested with delta9-THC. It was significant after 1 hr, maximally developed after 3 hr, and almost completely diminished after 6 hr. 11 references. (Author abstract)

183324 Krivoy, W.; Zimmermann, E.; Kroeger, D.; Taylor, A. N.; Branch, B. NIDA Addiction Research Center, P.O. Box 2000, Lexington, KY 40507 **Influence of tetracosactrin (T) and beta-melanocyte stimulating hormone (MSH) on depression of the segmental reflex by morphine (MS). (Unpublished paper).** Lexington, KY, NIMH, 1973. 1 p.

Experiments were performed to test the hypothesis that either tetracosactrin (T) or beta-melanocyte stimulating hormone (MSH) antagonize the depressant actions of MS on the segmental reflex of the decerebrate - spinal cat. Dorsal and ventral spinal roots were dissected and mounted on electrodes. Stimulation of the dorsal root evokes a reflex electrical response in the ventral root which was amplified, displayed on an oscilloscope and photographed for analysis. Five groups of animals were tested with a different treatment. After a 30 min control period, MSH, T or an equal volume of peptide vehicle was injected. One min later 12 cats received morphine (MS), followed at 30 min intervals by one of two larger doses. MSH augmented the monosynaptic potential but not the polysynaptic potential. T did not alter the evoked response. MS caused a significant decrease in mono and polysynaptic potentials, but did not cause a significant decrease of mono and polysynaptic potentials when preceeded by MSH or T. MS caused a significant decrease in blood pressure that was not modified by prior administration of MSH or T. Serum corticosteroid levels were high, variable, and did not change significantly in response to any of the drug treatments. (Author abstract modified)

183358 Ling, G. M.; Thomas, J. A.; Usher, D. R.; Singhal, R. L. Department of Pharmacology, Faculty of Medicine, University of Ottawa, Ottawa, Canada **Effects of chronically administered delta1-tetrahydrocannabinol of adrenal and gonadal activity of male rats.** Intern. J. of Clinical Pharmacology, Therapy and Toxicology (Munchen). 1(7):1-5, 1973.

The influence of chronically administered delta1-tetrahydrocannabinol (delta1-THC) on the activity of male rat adrenals and gonads was investigated, including analysis of corticosteriod production and thymus function following the injections. Daily administration of delta1-THC doses of 4 and 16mg/kg i.p. for 4 days exerted no significant effect on several organ weights, nor on the uptake of H3-testosterone by rat accessory sex organs, testes, adrenals, kidney, and liver. Whereas no change occurred either in the in vitro adrenal corticosteroid output or ACTH response, marked involution of the thymus gland was observed following treatment with delta1-THC, a principal psychoactive component of marihuana which has shown a wide variety of pharmacological effects. 18 references. (Author abstract)

183359 Caron, L. B.; Gauthier, R.; Pinard, G.; Gagnon, M.-A.; Tetreault, L. Department de Recherche Georges Villeneuve, Hopital St-Jean-de-Dieu, Montreal, Canada /**Influence of dibencycladine and imipramine on calorie intake and bodyweight.**/ Influence de la dibencycladine et de l'imipramine sur la prise de calories et le poids corporel. Intern. J. of Clinical Pharmacology, Therapy and Toxicology (Munchen). 7(1):37-43, 1973.

The influence of dibencycladine, or B.A. 34276 (Ludiomil) and imipramine on the calorie intake and bodyweight of acutely depressed patients was studied. The aim in studying the two antidepressants was to verify what the Ss ingested insofar as quality and quantity of food to determine more precisely the possible evolution of the acute depression from a dietary viewpoint. No significant difference between drugs was noted on the evolution of depressive behavior. All Ss showed an increase in weight during the acute phase. No statistical differences in the chronological evolution of calories ingested, nor of the proportion of carbohydrates or proteins, were shown. However, a significant difference between Ss receiving B.A. 34276 and those receiving imipramine was noted in spontaneous fat ingestion. Results gain further significance when combined with findings from laboratory experiments on animals and give support to a hypothesized toxic effect of B.A. 34276, further indicating that anorexia constitutes an early symptom of poisoning. 7 references. (Author abstract)

183363 Parker, J. M.; Dubas, T. C. University of Western Ontario, Department of Pharmacology, London, Ontario, Canada **Automatic determination of the pain threshold to electroshock and the effects of delta9-THC.** Intern. J. of Clinical Pharmacology, Therapy and Toxicology (Munchen). 7(1):75-81, 1973.

The effect of levorotary delta9-tetrahydrocannabinol (delta9-THC) on the pain threshold and escape response of rats in which electrodes were chronically implanted into regions of the brain considered to subserve pain sensation and response was investigated. The possible antinociceptive action of delta9-THC produced both a rise in the electroshock pain threshold as well as an attenuation of the escape response. This analgesic activity was not dose related and had a profile different from that of the narcotic analgesics. The medial lemniscus was the most sensitive to the drug's actions. It is suggested that the analgesia observed is related to the altered perceptual qualities so characteristic of marihuana and similar psychedelic compounds. 18 references. (Author abstract)

183519 Sinyukhin, V. N. S. Ordzhonikidze All Union Scientific Research Chemical Pharmaceutical Institute, Moscow /**The absorption and distribution of the new antidepressant azaphen in the organs.**/ Vsasyvaniye i raspredeleniye po organam novogo antidepressanta azafena. Farmakologiya i Toksikologiya (Moskva). 36(4):409-411, 1973.

The absorption and distribution of a tricyclic antidepressant azaphen 2-(methyl-piperazinyl-1)-10-3,4-diazephenoxasine in the organs of rats were studied. Azaphen was found to be well absorbed by the gastrointestinal tract with the bulk of the drug found in the liver and kidneys; lesser amounts were found in the heart and brain. A considerable quantity of the drug was deleted from the organism with the urine. 7 references. (Journal abstract modified)

183601 Misra, Radhey S.; Barthwal, Jayanti P.; Parmar, Surendra S.; Brumleve, Stanley J. Department of Pharmacology and Therapeutics, King George's Medical College, Lucknow University, Lucknow 3, India **Substituted benzoxazole/benzthiazole-2-thiones: interrelationship between anticonvulsant activity and inhibition of nicotinamide adenine dinucleotide-dependent oxidations and monoamine oxidase.** Journal of Pharmaceutical Sciences. 63(3):401-404, 1974.

3-Alkyl benzoate/benzhydrazide aminomethyl benzoxazole/benzthiazole-2-thiones were synthesized and evaluated for their ability to affect the respiratory activity of rat brain homogenate. All compounds were found to inhibit selectively the nicotinamide adenine dinucleotide (NAD) dependent oxidation of DL-isocitrate, alpha ketoglutarate, and pyruvate while NAD independent oxidation of succinate remained unaltered. Inhibition of monoamine oxidase by 3-benzhydrazide aminomethyl benzoxazole/benzthiazole was greater with benzthiazoles as compared to the corresponding benzoxazoles. Anticonvulsant activity exhibited by these benzoxazole/benzthiazole derivatives against pentylenetetrazol induced seizures was found to be unrelated to their enzyme inhibitory properties. 5 references. (Author abstract)

183608 Prepas, Stephen; Menon, M. K.; Clark, W. G. Psychopharmacology Research Laboratory, Veterans Administration Hospital, Sepulveda, CA 91343 **Effect of 3,4-dimethoxyphenethylamine on monoamine-depleted rats.** Journal of Pharmacy and Pharmacology (London). 25(8):659-660, 1973.

In a letter to the editor, the effect of 3,4-dimethyoxphenethylamine (DMPEA) on monoamine depleted rats is reported. The failure of atropine or methysergide to block DMPEA effect indicated that DMPEA did not act mainly by stimulating acetylcholine or 5-hydroxytrptamine receptors. DMPEA also clearly blocked the effects of lysergic acid diamide, l-dopa and apomorphine. It is concluded that the DMPEA rigidity is due to the blockade of the central nervous system dopamine system. 7 references.

183609 Carlini, E. A.; Leite, J. R.; Tannhauser, M.; Berardi, A. C. Setor de Psicofarmacologia, Escola Paulista de Medicina, Rua Botucatu, 862, 04023, Sao Paulo, Brazil **Cannabidiol and Cannabis sativa extract protect mice and rats against convulsive agents.** Journal of Pharmacy and Pharmacology (London). 25(8):664-665, 1973.

In a letter to the editor, the anticonvulsant activity of cannabidiol (CBD) and cannabis sativa extract on mice and rats is reported. Results indicated that CBD and extracts of cannabis sativa were able, respectively, to protect mice against the leptazol induced convulsions and deaths and to block audiogenic convulsions in rats in abstinence from previous barbitone sodium administration. 17 references.

183610 Shintomi, K.; Yamamura, M. Osaka Research Division, Biological Research Laboratory, Tanabe Seiyaku Co., Ltd., Higashiyodogawaku, Osaka, Japan **Effects of antiparkinsonian drugs on neuroleptic-induced extrapyramidal signs in monkeys.** Journal of Pharmacy and Pharmacology (London). 25(8):666-667, 1973.

In a letter to the editor, the effects of antiparkinsonian drugs on neuroleptic induced extrapyramidal signs in monkeys are reported. PG-501 as well as trihexyphenidyl showed a clear antagonistic effect on the haloperidol induced cataleptic features, while ethopropazine and benztropine were less antagonistic than trihexyphenidyl. Furthermore, PG-501 and trihexyphenidyl antagonized the perphenazine induced cataleptic features for more than 30 h. Benztropine produced less antagonistic activity over 6 h, but the moderate effect was observed 24 h after perphenazine injection. Ethopropazine also showed a moderate antagonistic effect on the perphenazine induced cataleptic features. 7 references.

183611 Kourounakis, P.; Szabo, S.; Selye, H. Institut de medicine et de chirurgie experimentales, Universit de Montreal, Montreal 101, Quebec, Canada **Effect of various steroids and ACTH on methyprylon plasma levels and sleeping time in rats.** Journal of Pharmacy and Pharmacology (London). 25(8):670-672, 1973.

In a letter to the editor, the effect of various steroids and ACTH on methyprylon plasma levels and sleeping time in rats is reported. The methyprylon concentration in the blood of rats given pregnenolone-16alpha-carbonitrile (PCN) or spironolactone was significantly lower than that of the non-recovered controls (killed when the pretreated animals regained the righting reflex); it corresponded to the level in recovered controls when the righting reflex reappeared in these rats. The significant reduction of methyprylon sleeping time in animals pretreated with these two steroids was associated with a fall in the plasma level of the drug, which seems to be due to hepatic microsomal enzyme induction. Methyprylon sleeping time was slightly decreased in fluorocortisol acetate treated rats, but the changes in the plasma concentration of the drug were not significant although they displayed a prophylactic pattern characteristic of steroids that enhance the detoxication of endogenous and exogenous toxicants via induction, activation, decreased degradation of drug metabolizing enzymes and/or accelerated substrate elimination. Both triamcinolone and ACTH significantly inhibited the action of methyprylon and, here, the increase in the blood level was not marked. Judging from the plasma concentration of the drug, these two compounds seemed to improve host - tissue tolerance by permitting coexistence with the pathogen (e.g.,by suppressing nonspecific inflammatory or allergic reactions against it). 20 references.

183682 Krendal, F. P.; Kudrin, A. N. Department of Pharmacology, Pharmaceutical Faculty, Moscow Medical Institute imeni I. M. Schenov, Moscow /**A comparative study of the antipsychotic action of some neuroleptics based on the model of LSD psychoses.**/ Sravnitel'noye issledovaniye antipsikhoticheskogo deystviya nekotorykh neyroleptikov na modeli LSD-psikhoza. Zhurnal Nevropatologii i Psikhiatrii imeni S.S. Korsakova (Moskva). 73(5):747-753, 1973.

Antipsychotic actions of aminazine, haloperidol, and droperidol based on the model of LSD psychosis, are reported and compared. Experiments were carried out on rabbits. Behavior, EEG data, respiration, electrocardiographic data and temperature were analyzed. It was established that derivatives of butyrophenones are better antagonists of LSD than

aminazine. The most effective antagonist of LSD which does not exert extrapyramidal disturbances is droperidol. It is concluded that although the use of haloperidol is very effective in combatting LSD psychosis, it must be used in combination with other drugs. 35 references. (Journal abstract modified)

183787 Ho, Beng T.; Taylor, Dorothy; Englert, Leo F. Texas Research Institute of Mental Sciences, Houston, TX **Effects of delta9-tetrahydrocannabinol on the metabolism of 3H-5-hydroxytryptamine and 3H-norepinephrine in the rat brain.** Research Communications in Chemical Pathology and Pharmacology. 7(4):645-650, 1974.

The effects of delta9-tetrahydrocannabinol (THC) on the metabolism of 3H-5-hydroxytryptamine (5-HT) and norepinephrine (NE) were examined in rat brain. Chronic administration of THC changed the metabolism of intracisternally injected 5-HT and NE. There was a reduction of the level of brain 3H-5-hydroxyindoleacetic acid and an elevation of that of labeled deaminated metabolites of NE in the THC treated animals; however, no change in the concentration of brain 3H-5-HT, 3H-NE and H-normetanephrine was observed. The opposite effect on the turnover of the two brain amines was suggested as basis for the psychoactive property of THC. 11 references. (Author abstract modified)

183788 Borgen, Lowell A.; Davis, W. Marvin. Department of Pharmacology, School of Pharmacy, University of Mississippi, University, MS 38677 **Cannabidiol interaction with delta9-tetrahydrocannabinol.** Research Communications in Chemical Pathology and Pharmacology. 7(4):663-670, 1974.

The effects of cannabidiol (CBD), a supposedly inactive marihuana constituent, on several actions of delta9-tetrahydrocannabinol (THC) were studied in rats. In rats, 25mg/kg of CBD given i.p. 30 min prior to 10mg/kg THC reduced the magnitude and duration of the hypothermic effects of THC, while CND alone had no effect on body temperature. CBD (25mg/kg, i.v.)given 1 hr before THC (3mg/kg, i.v.)to unanesthetized rabbits caused a significant attenuation of the depressant effects of THC on heartrate, respiration and rectal temperature. These data suggest that although CBD is relatively inactive compared to THC, it may be a potential competitive antagonist of the effects of THC. 8 references. (Author abstract)

183789 Cohn, Major L.; Cohn, Marthe; Taylor, Floyd H. Department of Anesthesiology, University of Pittsburgh School of Medicine, Pittsburgh, PA 15213 **Norepinephrine -- an antagonist of dibutryl cyclic AMP in the regulation of narcosis in the rat.** Research Communications in Chemical Pathology and Pharmacology. 7(4):687-699, 1974.

The effects of nonepinephrine (NE), an antagonist of dibutyryl cyclic AMP in the regulation of narcosis were examined in the rat. NE administered centrally to rats anesthetized with amobarbital prolonged narcosis. The higher doses of NE induced severe toxic symptoms followed by death. The addition of varying doses of dibutyryl adenosine 3',5'-monophosphate (db cyclic AMP) to NE reduced the duration of narcosis potentiated by the latter but did not alter the toxic symptoms of the higher doses. In the regulation of the duration of narcosis, the lack of analogy between the behavioral effects of exogenously administered NE and db cyclic AMP challenges the concept that the action of NE is mediated in the brain uniquely through a second messenger system. 32 references. (Author abstract)

183794 Javoy, F.; Agid, Y.; Bouvet, D.; Glowinski, J. Laboratire de Biologie Moleculaire, College de France, 11, place Marcelin Berthelot, Paris 5e, France **In vivo estimation of tyrosine hydroxylation in the dopaminergic terminals of the rat neostriatum.** Journal of Pharmacy and Pharmacology (London). 26(3):179-185, 1974.

A technique to distinguish dopamine synthesis from its release and utilization in dopamine terminals of the rat neostriatum (NCP) is reported. It enables a direct in vivo estimation of tyrosine hydroxylation, a rate limiting step in dopamine synthesis. Locally injected L-3,5(3H)tyrosine is converted to (3H)dopamine in the NCP. The conversion of the labelled tyrosine into (3H)dopa leads to local accumulation of (3H)water (3H-H2O). The initial accumulation of the 3H-H2O levels in tissues gives a good reflection of the rate of tyrosine hydroxylation occurring in the dopamine terminals of the nigro-striatal pathway. In effect, 3H-H2O formation disappeared after elective degeneration of the nigro-neostriatal dopamine neurons, was inhibited by alpha-methyl-p-tyrosine, and was not affected by intraperitoneal injection of urea, which is known to reduce brain water content. 3H-H2O accumulation was enhanced by various neuroleptic drugs and inhibited by (+)-amphetamine. Ro 4-4602 an inhibitor of dopadecarboxylase reduced 3H-H2O formation 30 min after its injection. 19 references. (Author abstract)

183795 Vollmer, R. R.; Cavero, I.; Ertel, R. J.; Solomon, T. A.; Buckley, J. P. Department of Pharmacology, College of Pharmacy, University of Houston, Houston, TX 77004 **Role of the central autonomic nervous system in the hypotension and bradycardia induced by (-)-delta9-tetrahydrocannabinol.** Journal of Pharmacy and Pharmacology (London). 26(3):186-192, 1974.

The role of the central adrenergic system in the hypotension and bradycardia induced by (-)-delta9-trans-tetrahydrocannabinol (THC) was examined in cats. THC, when given intravenously to cats, produced marked decreases in blood pressure and heartrate which developed gradually and were of prolonged duration. Cervical spinal transection abolished these effects whereas surgical removal of neurogenic tone to the myocardium selectively eliminated the bradycardia. Bilateral vagotomy alone did not modify the action of THC upon heartrate or blood pressure. Recordings of spontaneous sympathetic outflow in the inferior cardiac nerve indicated a rapid reduction in neural discharge rate after THC administration. The observations support the hypothesis that THC produces a cardiodecellerator and hypotensive effect by acting at some level within the sympathetic nervous system. Experiments conducted to investigate transmission in the superior cervical and stellate ganglia demonstrated that THC did not alter ganglionic function. The possible action of THC on central sympathetic structures was investigated by perfusion of THC into the lateral cerebral ventricle. THC produced a significant reduction in heartrate without a substantial lowering of blood pressure. 14 references. (Author abstract modified)

183797 Yehuda, Shlomo; Wurtman, Richard J. Laboratory of Neuroendocrine Regulation, Department of Nutrition and Food Science, MIT, Cambridge, MA 02139 **Paradoxical thermoregulatory behaviour in rats induced by (+)-amphetamine: blockade by alpha-adrenoceptor or dopamine receptor blocking agents.** Journal of Pharmacy and Pharmacology (London). 26(3):210-212, 1974.

The effects of propranolol and phenoxybenzamine on (+)-amphetamine induced paradoxical thermoregulatory behavior were examined in rats. Control animals placed in an environment at 4 degrees C moved towards the heat lamp, while (+)-

amphetamine treated animals moved in the opposite direction away from the heat lamp. Pretreatment of rats with phenoxybenzamine blocked the movement away from the heat lamp. The administration of BE-2254 (HEAT, 2-(beta(4-hydroxyphenyl)-ethyl-aminomethyl) tetralone), like phenoxybenzamine, blocked the amphetamine induced paradoxical behavior. By itself, it did not affect thermoregulatory behavior, but did produce hypothermia among rats kept at 4 degrees. It is concluded that the blockade of (+)-amphetamine induced paradoxical thermoregulatory behavior by alpha-adrenoceptor blocking agents is not mediated by their effects on 5-HT receptors. The possible effects of alpha-adrenoceptor blockers, such as phenoxybenzamine and BE-2254, on dopaminergic synapses were tested in two experimental behavior situations, stereotypy and rotational behavior. Neither drug blocked the stereosituations, stereotype and rotational behavior. Neither drug blocked the stereotyped behavior induced by either amphetamine or apomorphine. It is suggested that noradrenergic synapses exist in the pathway which mediates the amphetamine induced paradoxical behavior, and that the flow of signals across the synapses is blocked by alpha-adrenoceptor blocking agents. 8 references.

183866 Chinn, C.; Weber, L. J. Department of Psychological Sciences, Purdue University, West Lafayette, IN 47907 **The actions of several psychoactive agents upon the muscarinic mechanisms in the superior cervical ganglion of the cat.** Neuropharmacology (Oxford). 13(1):39-52, 1974.

In a chloralose - urethane anesthetized cat, the actions of several psychoactive agents upon the muscarinic mechanisms in the superior cervical ganglion were tested. Responses of the nictitating membrane to electrical stimulation of the preganglionic nerve and to ganglionic stimulants delivered to the ganglion via intraarterial injection were measured before and after several psychoactive agents were delivered to the ganglion in the same way. Methylphenidate, pheniprazine and desipramine specifically antagonized the response of 4-(m-chlorophenylcarbamoyloxy)-2-butynyltrimethylammonium chloride (McN-A-343) a muscarinic stimulant, but not the response of 1,1-dimethyl-4-phenyl-piperazinium iodide (DMPP), a nicotinic stimulant. In addition, the above antidepressants or psychostimulant antagonized muscarinic transmission but not nicotinic transmission in a sympathetic ganglion at the doses indicated. These results suggest a possible mode of action of antidepressants and psychostimulants in the brain to produce atropine like autonomic effects observed in man during clinical use of these drugs. 32 references. (Author abstract)

183868 Papeschi, R. Max-Planck-Institut fur Psychiatrie, Kraepelinstrasse 2, 8 Munchen 23, W. Germany **Amantadine may stimulate dopamine and noradrenaline receptors.** Neuropharmacology (Oxford). 13(1):77-83, 1974.

Amantadine was examined as a dopamine and noradrenaline receptor stimulant. Amantadine, injected at a long interval after alpha-methyl-p-tyrosine (MT), exerted a dose dependent long lasting antagonism of MT induced sedation, catalepsy, adipsia and aphagia; however, amantadine, under these experimental conditions, did not antagonize MT toxicity (unlike when the former drug is injected before MT) and aggravated MT hypothermia. No difference in the concentration of brain catecholamines was observed between controls and amantadine treated rats in these experiments. However, when amantadine was injected 1 hr before MT, a moderate retardation of the depletion of both catecholamines in the brain was observed; no significant changes of the baseline catecholamine concentrations were found after amantadine alone. It is suggested that amantadine possesses the property to stimulate catecholamine receptors in the brain, besides that of releasing catecholamines the former property is suggested to be important in behavioral experiments and in the treatment of Parkinson's disease, whilst the latter might partially obscure the former in biochemical experiments. 25 references. (Author abstract)

183869 Fuller, R. W.; Snoddy, H. D. Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN 46206 **Long-term effects of 4-chloroamphetamine on brain 5-hydroxyindole metabolism in rats.** Neuropharmacology (Oxford). 13(1):85-90, 1974.

The long-term effects of 4-chloroamphetamine on brain 5-hydroxyindole metabolism in rats were examined. Four weeks after a single intraperitoneal injection of 4-chloroamphetamine hydrochloride into rats, brain serotonin and 5-hydroxyindoleacetic acid levels were still depressed to approximately half the control values, though tryptophan levels in brain were normal. Serotonin turnover in brain was likewise depressed to about half of the control rate as measured by the rate of serotonin accumulation after monoamine oxidase inhibition and the rate of 5-hydroxyindoleacetic acid accumulation after probenecid administration to block its efflux. Despite this decreased turnover rate, the capacity of the brain to synthesize 5-hydroxyindoles, as indicated by the increases in serotonin and 5-hydroxyindoleacetic acid after the injection of various doses of L-tryptophan, was not altered. 20 references. (Author abstract)

183887 Hirsh, Kenneth; Wang, S. C. Department of Pharmacology, General Foods Corporation, Technical Center, White Plains, NY 10625 **Selective respiratory stimulating action of doxapram compared to pentylenetetrazol.** Journal of Pharmacology and Experimental Therapeutics. 189(1):1-11, 1974.

The effects of doxapram and pentylenetetrazol on medullary respiratory and nonrespiratory neurons were studied in midcollicular decerebrate cats. It was found that doxapram acts on two sites: the chemoceptors and the medullary neurons. The carotid chemoceptors are most sensitive to the drug. The observed 'selective' stimulation of medullary respiratory neurons evoked by small intravenous doses of 0.05 to 0.25mg/kg was due to indirect activation of these neurons through carotid chemoceptor activation. The aortic chemoceptors play a very minor role at these doses. The direct, central neuronal stimulation is effected by large doses of doxapram. This action is nonselective. It is interesting that although doxapram does not selectively stimulate the respiratory neurons per se, a selectivity for respiratory neuron activation was demonstrated over the entire dose range studied. When the dose is increased, both medullary respiratory and nonrespiratory neurons are directly and equally stimulated, but the stimulatory effect on respiratory neurons is augmented by additional input coming from the carotid chemoceptors. 25 references. (Author abstract modified)

183891 Stolk, Jon M.; Barchas, Jack D.; Goldstein, Michael; Boggan, William; Freedman, Daniel X. Dartmouth Medical School, Hanover, NH 03755 **A comparison of psychotomimetic drug effects on rat brain norepinephrine metabolism.** Journal of Pharmacology and Experimental Therapeutics. 189(1):42-50, 1974.

The effects of LSD, psilocybin, mescaline, amphetamine and cold water swimming stress on the metabolism of 3H-norepinephrine in rat brain were determined. Graded doses of LSD showed no specific effects on brain catecholamine

metabolism, suggesting that this drug had little direct activity on brain noradrenergic neurons. Psilocybin had effects similar to those obtained with amphetamine as evidenced by a prominent and sustained elevation in 3H-normetanephrine content. These findings are consistent with an increased release of norepinephrine from central nerve endings. Cold water swim stress, on the other hand, resulted in a profound increase in 3H-deaminated catechol metabolites, suggesting that the intracellular catabolism of norepinephrine was affected specifically. Mescaline had a biphasic effect on brain 3H-norepinephrine metabolism. Mescaline appears to cause an initial increase in intracellular 3H-norepinephrine metabolism, followed by a period of enhanced release similar to the effects of amphetamine and psilocybin. These data indicate that the psychotomimetic drugs tested share no single common effect on brain norepinephrine metabolism. 35 references. (Author abstract modified)

183894 Buchenauer, Doris; Turnbow, Marilyn; Peters, Marvin A. Department of Pharmacology, School of Medicine, Loma Linda University, Loma Linda, CA 92354 **Effect of chronic methadone administration on pregnant rats and their offspring.** Journal of Pharmacology and Experimental Therapeutics. 189(1):66-71, 1974.

The effects of chronic methadone administration on pregnant rats and their offspring were studied. Treatment of the female during pregnancy resulted in a decreased number of live offspring per litter, an increase in the percentage of stillborn pups, an increase in infant mortality and a retardation of growth of the pups nursing treated mothers. There was a dose response relationship in most parameters at the lower doses used but at higher dose levels the dose response was not as obvious. The overall effect of methadone on reproduction was seen as an increase in the number of maternal deaths, a decrease in the number of pups born per litter and a decrease in the number of pups weaned. 11 references. (Author abstract modified)

183895 Cicero, Theodore J.; Meyer, Edward R.; Smithloff, Ben R. Department of Psychiatry, 4940 Audubon Ave., St. Louis, MO 63110 **Alpha adrenergic blocking agents: antinociceptive activity and enhancement of morphine-induced analgesia.** Journal of Pharmacology and Experimental Therapeutics. 189(1):72-82, 1974.

The effects of reducing the activity of norepinephrine in the nervous system, either by depleting endogenous levels via dopamine-beta-hydroxylase inhibition or blocking its effects at the receptor level, on hot plate reaction time and morphine's analgesic activity were determined in rats. Inhibition of dopamine-beta-hydroxylase resulted in a significant prolongation of morphine's antinociceptive activity on the hot plate. The alpha adrenergic blocker, phenoxybenzamine, alone produced a nearly two fold increase in reaction time on the hot plate when a dose of 10mg/kg was administered 22 hours prior to testing. In rats pretreated with phenoxybenzamine, the effect of a minimally effective dose of morphine on hot plate reaction time was significantly enhanced, both in terms of the initial increase in reaction time after the administration of the narcotic and the duration of its antinociceptive activity. The combined effect of phenoxybenzamine and morphine on hot plate reaction time was substantially greater than that which would be predicted simply on the basis of an addition of the two drugs' effects. The results suggest that the actions of morphine and related narcotics may be associated with a reduction in norepinephrine's activity in the nervous system particularly at alpha adrenergic receptor sites. 34 references. (Author abstract modified)

183896 Ciofalo, Frank R. School of Medicine, Anderson Health Sciences Building, University of Nevada, Reno, NV 89507 **Methadone inhibition of 3H-5-hydroxytryptamine uptake by synaptosomes.** Journal of Pharmacology and Experimental Therapeutics. 189(1):83-89, 1974.

Methadone inhibition of 3H-5-hydroxytryptamine (5-HT) uptake by synaptosomes prepared from whole rabbit brain by differential centrifugation and sucrose Ficoll gradients is reported. Methadone dramatically inhibited 5-HT uptake by synaptosomes. Morphine also inhibited 5-HT uptake by synaptosomes but only at relatively high concentrations. Naloxone decreased 5-HT uptake by synaptosomes. Naloxone partially blocked the effect of methadone but not the effect of morphine on 5-HT uptake. Neither methadone nor morphine altered KCl stimulated 5-HT release from preloaded synaptosomes. The results suggest that narcotic inhibition of 5-HT uptake by nerve terminals is not involved in analgesic mechanisms and is not due to reaction with the specific opiate receptor. However, the marked effects of methadone on 5-HT uptake may possibly be related to this compound's actions and relatively long-lasting effects in vivo. 18 references. (Author abstract modified)

183897 Gessner, Peter K.; Clarke, Carolyn C.; Adler, Michael. 122 Capen Hall, SUNY at Buffalo, Buffalo, NY 14214 **The effect of low environmental temperature on the tranylcypromine-meperidine interaction in mice.** Journal of Pharmacology and Experimental Therapeutics. 189(1):90-96, 1974.

The effect of a low environmental temperature on the mortality resultant from the administration of tranylcypromine and meperidine 4 hours apart was investigated in mice. It was found that exposure to an environmental temperature of 2 degrees C for 1 hour prior to meperidine administration markedly reduced mortality among animals removed from the low temperature environment after the meperidine administration and markedly increased mortality among animals continued at the low temperature, after meperidine administration. Because the tranylcypromine - meperidine interaction is normally associated with a marked hyperthermia, the body temperature correlates of the interaction were investigated in mice exposed to a low environmental temperature. Under the conditions of cold exposure, mice administered tranylcypromine and meperidine did not show a hyperthermic response but rather a hypothermic one. Further investigation showed this response to be mediated exclusively by meperidine. In related experiments intertreatment with prednisolone was found to be without effect on the mortality resultant from the tranylcypromine - meperidine interaction. 32 references. (Author abstract)

183899 Abrams, Larry S.; Elliott, Henry W. Department of Medical Pharmacology and Therapeutics, California College of Medicine, University of California, Irvine, CA **Morphine metabolism in vivo and in vitro by homozygous Gunn rats.** Journal of Pharmacology and Experimental Therapeutics. 189(1):285-292, 1974.

In a study of morphine metabolism in vivo and in vitro, adult homozygous Gunn and Wistar rats were given daily injections with subcutaneous doses of morphine sulfate starting at 20mg/kg and gradually increasing to 35mg/kg over a 30 day treatment period. No differences were found between Gunn and Wistar rats in the average urinary excretion of conjugated morphine during the treatment period. Incubation of the urine of morphine treated rats with beta-glucuronidase provided no evidence to support the existence of any morphine conjugate

other than glucuronide. The percentage of dose recovered as urinary conjugated morphine was not decreased by chronic morphine treatment of either Gunn or Wistar rats but the percentage recovered as free morphine was increased significantly more in Gunn than in Wistar rats. No significant differences were observed between Gunn and Wistar rat uridine diphosphate glucuronyltransferase activity when hepatic microsomes from adult Gunn and Wistar rats were incubated with morphine and uridine diphosphate glucuronic acid. Subsequent hydrolysis of the product with beta-glucuronidase indicated that the morphine conjugate formed with a glucuronide. 42 references. (Author abstract modified)

184178 Asano, Yutaka; Moroji, Takashi. Department of Psychiatry and Neurology, Hokkaido University School of Medicine, Sapporo, Japan **Effects of methamphetamine on daily rhythms of hypothalamic norepinephrine, serotonin and plasma corticosterone levels in the rat.** Life Sciences. 14(8):1463-1472, 1974.

The relationship between daily rhythms of hypothalamic norepinephrine (NE) and serotonin (5HT) contents and the circadian rhythm of plasma corticosterone (Comp.B) levels was studied in the rat. It was found that levels of hypothalamic NE, 5HT and plasma Comp.Bexhibited distinct daily fluctuations in the control condition. In animals treated with methamphetamine, the daily rhythms of hypothalamic 5HT contents and plasma Comp. B levels remained unchanged, whereas the daily rhythm of hypothalamic NE contents was completely abolished. It was suggested that the daily rhythm of hypothalamic NE is not functionally related to the circadian change of pituitary - adrenocortical activity. 28 references. (Author abstract)

184179 Brase, David A.; Tseng, Liang-Fu; Loh, Horace H.; Way, E. Leong. Langley Porter Neuropsychiatric Institute, San Francisco, CA 94143 **Cholinergic modification of naloxone-induced jumping in morphine dependent mice.** European Journal of Pharmacology (Amsterdam). 26(1):1-8, 1974.

The effects of several i.p. administered, centrally active cholinergic agonists and antagonists on the naloxone induced jumping behavior of morphine tolerant and dependent mice were studied in an effort to differentiate muscarinic and nicotinic modification of the withdrawal jumping behavior. Nicotine, tremorine, oxotremorine, arecoline and physostigmine significantly inhibited jumping, whereas atropine, benzotropine, pempidine and mecamylamine significantly potentiated jumping. Quaternary cholinergic drugs did not modify jumping. These drug effects were obtained generally without an alteration of the amount of naloxone or morphine in the brain. Cholinergic drugs also modified the jumping incidence in mice undergoing abrupt morphine abstinence. It is concluded that the inhibition of withdrawal jumping in morphine dependent mice by both muscarinic and nicotinic agonists and its enhancement by muscarinic and nicotinic antagonists reflect cholinergic modifications of the jumping response by a central mechanism(s). 25 references. (Author abstract)

184180 Buening, Mildred K.; Gibb, James W. Department of Pharmacology, Colleges of Medicine and Pharmacy, University of Utah, Salt Lake City, UT 84132 **Influence of methamphetamine and neuroleptic drugs on tyrosine hydroxylase activity.** European Journal of Pharmacology (Amsterdam). 26(1):30-34, 1974.

The influence of methamphetamine and neuroleptic drugs on tyrosine hydroxylase (TH) activity was examined in rats. After rats had been treated with drugs for 36 hr, striatal and adrenal TH activities were determined by the coupled decarboxylase method. Treatment with methamphetamine 10mg/kg, s.c.,depressed striatal TH activity but elevated adrenal enzyme activity. Neither chlorpromazine nor haloperidol affected TH activity in the striatum; however, when either of these neuroleptic drugs was administered concurrently with methamphetamine, the depression of striatal enzyme activity produced by methamphetamine was prevented. Adrenal enzyme activity was increased by chlorpromazine 15mg/kg, i.p.;when this dose was administered concurrently with methamphetamine, the enzyme activity was greater than that produced by either drug alone. In contrast to chlorpromazine, haloperidol 5mg/kg, i.p.,had no effect on adrenal TH activity and seemed to impair the elevation produced by methamphetamine. 15 references. (Author abstract)

184197 Haefely, W. Abt. fur Experimentelle Medizin, F. Hoffmann-La Roche & Co., CH-4002 Basel, Switzerland **The effects of 5-hydroxytryptamine and some related compounds on the cat superior cervical ganglion in situ.** Archives of Pharmacology (Berlin). 281(2):145-165, 1974.

The effects of 5-hydroxytryptamine (5-HT) and related indole derivatives injected as i.a. bolus injections in a large dose range were studied in the cat superior cervical ganglion (SCG) by recording ganglionic and postganglionic electrical activity. 5-HT had two independent and opposite actions: 1) a long-lasting inhibition of ganglionic transmission occurred already with extremely low doses and increased up to highest ones; 2) both presynaptic and postsynaptic sites of action seem to be involved. In a medium and high dose range, the inhibitory effect was temporarily masked by a short lasting stimulation and a depolarization which was small when compared with that produced by nicotinic agents. The depolarization triggered a secondary hyperpolarization. The stimulant, but not the inhibitory action was very prone to tachyphylaxis. Lysergic acid diethylamide, methysergide, psilocybin and N,N-dimethyltryptamine (DMT) possess only the inhibitory property of 5-HT. The two N,N-dimethylated derivatives bufotenine and DMT, as well as the alpha-methylated 5-HT stimulated nicotinic receptors, bufotenine in addition to, and 5-hydroxy-alpha-methyltryptamine in the absence of typical 5-HT like inhibitory and excitatory activity. Tryptamine had neither inhibitory nor excitatory 5-HT like actions, it depolarized and blocked transmission by an unknown mechanism. 30 references. (Author abstract modified)

184198 Kuschinsky, K. Max-Planck-Institut fur Experimentelle Medizin, Abt. Biochemische Pharmakologie, D-3400 Gottingen, Hermann Rein-Str. 3, Germany **Are cholinergic mechanisms involved in morphine effects on motility?** Archives of Pharmacology (Berlin). 281(2):167-173, 1974.

The relevance of cholinergic mechanisms in morphine induced effects on striatal dopamine metabolism and on motility were examined in rats and mice. In rats, atropine slightly decreased the striatal homovanillic acid (HVA) concentration, but affected neither the morphine induced rise of HVA concentration nor the catalepsy after morphine. In mice, even high doses of atropine induced only a moderate locomotor activity, compared with that observed after morphine application. The combination of morphine and atropine on locomotor activity seemed to be supraadditive. Although physostigmine antagonized the morphine induced locomotor activity, the results suggest that primary effects of morphine on cholinergic mechanisms in brain are of minor importance in inducing an increase of striatal dopamine turnover and effects on motility of rats and mice. 18 references. (Author abstract)

184199 Jend, H. -H.; Coper, H. Institut fur Neuropsychopharmakologie, D-1000 Berlin 19, Ulmenallee 30, Germany **On the mechanism of the synergistic effect of perazine and hexobarbital.** Archives of Pharmacology (Berlin). 281(2):219-232, 1974.

The synergistic effect of perazine and hexobarbital was studied in rats by interference with drugs which alter the adrenergic, serotonergic and cholinergic systems. The determination of hexobarbital level in blood and brain was used as an indication of the rate of its biotransformation. Findings indicated that perazine, dihydroergotamine (DHE), and phentolamine (in low doses) as well as an elevation of dopamine level prolong the anesthesia by way of a central mechanism. Phentolamine (in higher doses) and the anticholinergic drug biperidin slowed down the metabolism of hexobarbital. An alteration of the overall level of catecholamines, serotonin and acetylcholine had no effect on the hexobarbital induced anesthesia. The mild hyperthermia caused by all drugs tested, did not influence the duration of hexobarbital sleeping time. The possibility that perazine, like other alpha-receptor blocking agents, causes a preponderance of inhibitory dopaminergic neurons by obstructing the excitatory norepinephrine receptors in the central nervous system is discussed. This effect might also occur if the dopamine level in the brain is increased. 41 references. (Author abstract)

184201 Snider, Stuart R.; Waldeck, Bertil. Department of Neurology, College of Physicians and Surgeons, Columbia University, New York, NY **Increased synthesis of adrenomedullary catecholamines induced by caffeine and theophylline.** Archives of Pharmacology (Berlin). 281(2):257-260, 1974.

The increased synthesis of rat adrenomedullary catecholamines induced by caffeine and theophylline is reported. Caffeine or theophylline, 20mg/kg i.p.,was given to rats. Thirty minutes after the injection of either drug, adrenal dopamine increased 80 and 50%, respectively. This increase was prevented by a C-7 spinal cord transection made 24 h before. In transected animals adrenal dopamine decreased after caffeine; no statistically significant decreases in adrenaline + noradrenaline were observed. It is concluded that caffeine and theophylline activate the tyrosine hydroxylase by a mechanism which depends on a normal or increased nerve impulse flow. Release of adrenal catecholamines may occur both via neurogenic stimulation and directly. 9 references. (Author abstract)

184202 Haefely, W. Abteilung fur Experimentelle Medizin, F. Hoffmann-La Roche & Co., CH-4002, Basel, Switzerland **The effects of various 'nicotine-like' agents in the cat superior cervical ganglion in situ.** Archives of Pharmacology (Berlin). 281(1):93-117, 1974.

The effects of nicotine, lobeline, anabasine, cytisine, coniine, sparteine, piperidine, acetylcholine, tetramethylammonium (TMA) and dexamphetamine, were studied in the cat superior cervical ganglion (SCG) in situ and compared with those of (DMPP) 1,1-dimethyl-4-phenyl-piperazinium. A non-selective conductance increase of the ganglion cells by stimulation of nicotinic receptors is responsible for depolarization, firing, facilitation of ganglionic transmission and depolarization block. Changes in membrane potential, ganglionic conductivity and the sodium pump under various drug regimens are considered as are blocking and sensitization of nicotinic receptors. 35 references. (Author abstract modified)

184222 Greven, J. Abteilung Pharmakologie, Medizinische - Theoretisches Institut D-5100 Aachen, Melatener Strasses 213, Germany **Evidence for redistribution of filtrate among nephrons after beta- adrenergic stimulation and blockade.** Archives of Pharmacology (Berlin). 282(2):171-180, 1974.

Renal excretion of fluid and electrolytes, total kidney glomerular filtration rate (GFR) and superficial nephron GRF were determined in 42 Sprague Dawley rats after beta-adrenergic stimulation with isoprenaline and beta-adrenergic blockade with propranolol. Isoprenaline decreased urine volume, sodium and potassium excretion and increased urinary sodium and potassium concentration and urine osmolarity. These effects were reversed by injection of propranolol. Propranolol alone increased renal sodium and potassium excretion and urinary sodium concentration. Total kidney GFR did not change after both substances, whereas superficial nephron GFR increased after propranolol by 35%. It is suggested that a redistribution of glomerular filtration rates among nephrons therefore occured with a shift of the GFR to deep nephrons after isoprealine and to superficial nephrons after propranolol. 36 references. (Author abstract modified)

184223 Temple, Diana M.; Hasselbach, W.; Makinose, M. Department of Pharmacology, University of Sydney, Sydney 2006, Australia **The inhibition by beta-adrenoceptor blocking agents of calcium uptake into and efflux from isolated sarcoplasmic vesicles.** Archives of Pharmacology (Berlin). 282(2):187-194, 1974.

The inhibition by beta-adrenergic blocking agents of calcium uptake and efflux from isolated sarcoplasmic vesicles isolated from rabbit skeletal muscle is reported. The rates of calcium uptake and the calcium dependent increase in ATPase activity of sarcoplasmic reticulum vesicles isolated from rabbit skeletal muscle are reduced in the same ratio by the beta-adrenoceptor blocking agents propranolol, pronethalol and Ro-033528, but neither by practolol, sotalol nor oxprenolol. The total calcium accumulated was affected by none of the inhibitors. The inhibitory potency of these compounds upon the calcium pump appears to be correlated with their membrane activity or potency as local anesthetic agents, rather than with their beta-adrenoceptor blocking potency. 17 references. (Author abstract modified)

184225 Puri, Surendra K.; Lal, Harbans. Department of Pharmacology, and Toxicology, College of Pharmacy, University of Rhode Island, Kingston, RI 02881 **Tolerance to the behavioral and neurochemical effects of haloperidol and morphine in rats chronically treated with morphine or haloperidol.** Archives of Pharmacology (Berlin). 282(2):155-170, 1974.

Tolerance to the behavioral and neurochemical effects of haloperidol and morphine in rats chronically treated with morphine or haloperidol is reported. The acute administration of morphine sulfate or haloperidol produced catalepsy and concomitant increase in striatal dopamine turnover in rats. The animals made dependent on morphine by 52 morphine injections and then tested during 3 days of withdrawal from morphine, showed tolerance to the cataleptic and the neurochemical effects of morphine as well as those of haloperidol. That tolerance was not seen after 14 days of withdrawal from morphine. The animals chronically treated with haloperidol for 12 days and then tested 72 h after last haloperidol injection, did not show tolerance to the cataleptic or the neurochemical effect of haloperidol or morphine. The results suggest that dopaminergic systems underlying motor coordination and regulation of the neurotransmitter synthesis are among those susceptible to narcotic action and to the process of tolerance development during narcotic dependence. 33 references. (Author abstract)

184226 Seiler, K.-U.; Wasserman, O. Institut fur Pharmakologie, Christian Albrechts-Universitat, D-2300 kiel, Hospitalstrasse 4-6, Germany **Evidence for an unusual distribution of chlorphentermine in vivo: an autoradiographic study in mice.** Archives of Pharmacology (Berlin). 282(2):113-122, 1974.

Evidence for an unusual distribution of chlorphentermine in mice is presented. 3H-Chlorphentermine is selectively taken up by secreting tissues, the reticuloendothelial and lymphatic system and other lipid rich organs, like central nervous system, retina and lungs. Considerable amounts are still present at least 1 week after a single i.v. injection. The extensive binding of chlorphentermine in these lipid or phospholipid rich organs is probably due to strong complex formation between this drug and phospholipids. Comparison of this distribution pattern with that of other amphiphilic drugs of related structure (halogenated aralkylamines) suggests that a general mechanism might be involved. 23 references. (Author abstract)

184227 Borbely, Alexander A.; Baumann, Isabel R.; Waser, Peter G. Pharmakologisches Institut der Universitat Zurich, CH-8006 Zurich, Gloriastrasse 32, Switzerland **Amphetamine and thermoregulation: studies in the unrestrained and curarized rat.** Archives of Pharmacology (Berlin). 281(4):327-340, 1974.

The effect of (+)-amphetamine on body temperature in the unrestrained and curarized rat was studied. In the unrestrained animal kept at an ambient temperature of 30 degrees C amphetamine had a dose dependent hyperthermic action, whereas in animals kept at 7 degrees C it decreased body temperature. An increase in body temperature was evident also in the curarized rat; after spinal cord transection at the level of C1; and in the pithed rat. Pretreatment with the alpha-adrenergic blocking agent azapetine attenuated amphetamine hyperthermia in the curarized rat, but enhanced the hyperthermic response in the unrestrained rat. Pretreatment with the beta-adrenergic blocking agent propranolol abolished amphetamine hyperthermia in the curarized rat, but did not affect the response in the unrestrained animal. In the hypophysectomized animal amphetamine had a hypothermic effect even at high ambient temperatures. It is concluded that the action of amphetamine on peripheral beta-receptors has a hyperthermic effect, but that additional mechanisms are involved in the thermal response of the freely moving animal. 25 references. (Author abstract modified)

184228 Schlede, Eva; Borowski, R. Institut fur Pharmakologie der Freien Universitat D-1000 Berlin 33, Germany **Decreased effect of phenobarbital treatment on microsomal drug metabolizing enzyme activity during gestation.** Archives of Pharmacology (Berlin). 281(4):341-355, 1974.

The effects of phenobarbital treatment on microsomal drug metabolizing activity during gestation were studied in rats. Pregnant and nonpregrant rats were treated with phenobarbital (PB) twice daily for 4 days. Treatment resulted in a 35% increase in liver weight in nonpregnant rats. The livers of pregnant rats weighed the same as the livers from PB treated nonpregnant rats, and PB treatment during gestation had only a small stimulatory effect on liver weight. In liver microsomes, the Km and Vmax values were measured for the ethylmorphine N-demethylase and benzo(a)pyrene hydroxylase. For the two substrates the Km values were identical in all groups. The Vmax values for the two enzyme activities were not different in control pregnant and control nonpregnant rats when calculated per total liver. Treatment of the rats with PB increased the Vmax values for the two enzyme activities, but these values were significantly lower in the microsomes obtained from PB treated pregnant rats. The content of cytochrome P-450 was higher in PB treated nonpregnant rats than in control nonpregnant rats, but no increase in the amount of cytochrome P-450 was measured after treating pregnant rats with PB. 26 references. (Author abstract modified)

184229 Puig, M.; Bartholini, G.; Pletscher, A. Universidad de Barcelona, Departamento de Farmacologia & Terapeutica, Barcelona, Spain **Formation of noradrenaline in the rat brain from the four stereoisomers of 3,4-dihydroxyphenylserine.** Archives of Pharmacology (Berlin). 281(4):443-446, 1974.

The formation of noradrenaline (NA) in the rat brain from the four stereoisomers of 3,4-dihydroxyphenylserine (DOPS) is reported. Intraperitoneal injection of the (+)-erythro isomer of DOPS to rats markedly increased the concentration of cerebral NA which probably corresponds to the unnatural (+) form. In contrast, the other three stereoisomers of DOPS caused only a minor rise of NA. It is suggested that this difference is connected with the configuration of the stereoisomers at the alpha and beta carbon which determines the rate of decarboxylation and possibly of penetration into the brain. 13 references. (Author abstract)

184230 Philippu, A.; Glowinski, J.; Besson, M. J. Institut fur Pharmakologie und Toxikologie der Universitat, 87 Wurzburg, Koellikerstrasse 2, Germany **In vivo release of newly synthesized catecholamines from the hypothalamus by amphetamine.** Archives of Pharmacology (Berlin). 282(1):1-8, 1974.

In vivo release of newly synthesized catecholamines from the cat hypothalamus by amphetamine is reported. The posterior hypothalamus of cats immobilized with gallamine was superfused through a push - pull cannula with artificial cerebrospinal fluid. Addition of 3H-tyrosine into the superfusing fluid led to synthesis of 3H-catecholamines which were released spontaneously. Separation of the 3H-catecholamines by column chromatography or their acetylation and separation by paper chromatography revealed that both 3H-noradrenaline and 3H-dopamine were released. In most experiments 3H-noradrenaline represented about 10 to 25% of total 3H-catecholamines. Superfusion of the hypothalamus with amphetamine enhanced the release of total 3H-catecholamines, the release of 3H-noradrenaline being relatively more enhanced than that of 3H-dopamine. Determination of the readioactive compounds in the hypothalamus at the end of the experiments showed that total 3H-catecholamines represented 3% of 3H-tyrosine. About 15% of the total 3H-catecholamines were due to 3H-noradrenaline and 85% to 3H-dopamine. 15 references. (Author abstract)

184232 Lemmer, B; Saller, R. Zentrum der Pharmacologie, der J. W. Goethe-Universitat, D-6000 Frankfurt am Main, Germany **The effects of acute administration of propranolol and practolol on the uptake, content, release and turnover of noradrenaline in the rat heart in vivo.** Archives of Pharmacology (Berlin). 282(1):85-96, 1974.

The effect of the acute administration of propranolol and practolol, on the cardiac turnover of noradrenaline was studied in male Wistar rats kept under controlled conditions of environmental lighting. Propranolol caused no or only minor effects on the turnover in concentrations of 0.001-0.1mmoles/kg, whereas higher doeses (0.2-0.4mmoles/kg) decreased the noradrenaline turnover in rat hearts concomitantly with toxic signs from the central nervous system. The endogenous noradrenaline content was not changed by any concentration of propranolol. Practolol(0.1-0.4mmoles/kg) did not influence the cardiac noradrenaline turnover, but, like an indirectly act-

ing sympathomimetic drug, released noradrenaline. 38 references. (Author abstract)

184235 Graham, John M., Jr.; Schreiber, Robert A.; Zemp, John W. Department of Biochemistry, Medical University of South Carolina, Charleston, SC 29401 **Effect of D-amphetamine sulfate on susceptibility to audiogenic seizures in DBA/2J mice.** Behavioral Biology. 10(2):183-190, 1974.

The effect of D-amphetamine sulfate on susceptibility to audiogenic seizures in DBA/2J mice was studied. D-Amphetamine sulfate in saline was injected intraperitoneally into mice in doses of 0.25-16.0mg/kg. Fifteen minutes after injection, 21 or 26-day-old DBA/25 mice were tested for susceptibility to audiogenic seizures. Maximal protection was found at 1.0-2.0mg/kg at both ages. Fewer 21-day-old animals died after the maximally effective dose, and at 26 days old fewer animals manifested a wild running response than did saline controls. D-Amphetamine sulfate (2.0mg/kg) was then injected intraperitoneally, into DBA/2J mice at 21, 24, 27, 30, or 45 days old. Fifteen minutes after injection, each mouse was tested for susceptibility to sound-induced seizures. DBA/2J mice receiving D-amphetamine sulfate manifested significantly fewer severe seizures than control mice at 21, 24, and 27 days. In particular, the incidence of tonic seizures and death was significantly reduced for each of the age groups. For the 27-day-old mice, the incidence of clonic seizures was also significantly reduced. 19 references. (Author abstract)

184243 Gibson, T. P.; Ketter, K. A.; Delle, M.; DiBona, G. F. Department of Internal Medicine, University of Iowa College of Medicine, Iowa City, IA **Enhanced renal tubular secretion of meprobamate: role of saline-furosemide diuresis.** Clinical Toxicology. 7(1):29-35, 1974.

The role of saline - furosemide diuresis on enhanced tubular secretion of meprobamate was examined in dogs. The addition of furosemide to a steady state saline diuresis resulted in a significant increase in urine flow rate (V) and a significant decrease in C. Whole plasma meprobamate clearance and the clearance of ultrafilterable meprobamate were significantly increased by the addition of furosemide. Of the total plasma concentration of meprobamate, 66.9% was ultrafilterable during the saline periods and 66.7% was ultrafilterable during the saline - furosemide periods. The clearance ratios were significantly increased by the addition of furosemide. In three of five dogs the ratio of the clearance of ultrafilterable meprobamate to the clearance of inulin exceeded 1.0; 1.29, 1.13, and 1.14; the other two were 0.92 and 0.81. This is indicative of net tubular secretion of meprobamate. The finding of net tubular secretion of meprobamate under these conditions suggests that the kidney handles meprobamate by the processes of glomerular filtration, tubular reabsorption, and tubular secretion. 5 references.

184329 Clouet, Doris H. New York State Drug Abuse Control Commission, Testing and Research Lab., 80 Hanson Place, Brooklyn, NY 11217 **Dopamine in brain function.** Journal of the Formosan Medical Association (Taipei). 72 (11):44-52,1973.

The function of the neurotransmitter dopamine in the central nervous system is discussed. The dopamine uptake system in the retina, caudate nucleus, and other striatal regions is considered. Abnormal behavior patterns in experimental animals induced by drugs which stimulate the striatal dopamine receptor are described. The pharmacological action of the major tranquillizers and of opiates is discussed in terms of the effect on the dopamine uptake system. 13 references. (Journal abstract modified)

184372 Vernadakis, Antonia; Robb, Douglas. Dept. of Psychiatry, University of Colorado Medical Center, Denver, CO 80220 **Effects of amphetamine on electroshock responses in developing rats.** Developmental Psychobiology. 7(1):89-95, 1974.

Convulsive responses were studied after chronic and acute amphetamine treatment in developing rats. Under chronic treatment, 27 litters of male rats received d-amphetamine either at 3-6, 8-11, or 22-25 days after birth and the electroshock seizure threshold (EST) was studied during maturation; each litter consisted of controls and rats treated with 1, 3, or 6mg/kg body weight amphetamine. Under acute treatment, groups of rats (16 per group) received amphetamine 45 min before electroshock testing at 8, 16, or 25 days after birth. The EST was significantly higher for the first week after treatment in rats given amphetamine (3mg/kg) from 8-11 days after birth; no changes were observed in the other groups tested chronically with amphetamine. The EST was lower in rats treated acutely at 8 or 16 days and higher in rats treated at 25 days. These data demonstrate that the effects of amphetamine on convulsive responses are dependent not only on the stage of central nervous system (CNS) maturation at the time of drug administration, but also on the duration of drug treatment. 20 references. (Author abstract)

184553 Cheney, D. L.; Trabucchi, M.; Racagni, G.; Costa, E. NIMH, Bethesda, MD 20014 **Effects of various morphine treatment schedules on acetylcholine turnover rate in rat brain parts.** Bethesda, MD, NIMH, 1974. 1 p.

The effects of various morphine treatment schedules on acetylcholine (ACh) turnover rate in brain parts was determined in the striatum and occipital cortex of rats under the following conditions: 1) acute morphine; 2) naloxone; 3) naloxone and acute morphine; 4) chronic morphine; and 5) naloxone and chronic morphine. None of the conditions affected the steady state concentrations of ACh or choline (Ch). Actue morphine reduced the ACh turnover rate in the occipital cortex but not the striatum. Naloxone alone had no effect but reversed the effect of acute morphine in the occipital cortex. Chronic morphine decreased the ACh turnover rate in the striatum but not the cortex, while naloxone immediately reversed this effect in the striatum. Modulation of the cholinergic systems by dopaminergic neurons which are affected by morphine might explain differences in ACh turnover rate in the two brain areas. (Author abstract modified)

184839 Cole, Sherwood O.; Gay, Patricia E. Dept. of Psychology, Rutgers University, Camden, NJ 08102 **Brain mechanisms underlying the effects of amphetamine on feeding and nonfeeding behaviors: dissociation and overlap.** Physiological Psychology. 2(1):80-88, 1974.

Evidence is presented to support the view that there is one major distinction in the brain processes underlying the effects of amphetamine in feeding and nonfeeding behaviors. Amphetamine in feeding involves a final adrenergic blocking action in the lateral hypothalamus and in nonfeeding involves a facilitation of aminergic processes. Although the the primary processes underlying the effects of amphetamine on feeding and nonfeeding behavior are basically different, evidence suggests that there is considerable overlap in the complete central systems (primary and modulatory) involved in such mediations. Suggestions for further research are presented which are consistent with these distinctions in central mechanisms. 97 references. (Author abstract modified).

184975 Torre, Michele; Bogetto, Filippo; Torre, Eugenio. Department of Psychiatry and Psychopharmacology, Via Cherasco 15, I-10126 Torino, Italy **Effect of LSD-25 and 1-methyl-d-lysergic acid butanolamide on rat brain and platelet serotonin levels.** Psychopharmacologia (Berlin). 36(2):117-122, 1974.

The effect of LSD-25 and l-methyl-d-lysergic acid butanolamide (UML) on rat brain and platelet serotonin levels was investigated. Factorial analysis of rat cerebral serotonin (5-HT) values observed following intraperitoneal LSD-25 and UML showed that the highly significant decrease induced by both drugs was independent of dose and that the effect of both drugs was the same. Increased platelet 5-HT values were also obtained with each drug. These findings suggest that the psychotomimetic effect of LSD-25 is not due to changes in cerebral 5-HT, since a relationship can probably be postulated between such an effect in man and the effect of LSD-25 on conditioned behavior in the rat. It is also felt that the fact that these drugs decrease and increase cerebral and platelet values respectively may be of assistance in the interpretation of data relating to platelet 5-HT patterns in man under psychiatric conditions and during treatment with psychotropic drugs. 16 references. (Author abstract modified)

185112 Roizin, L.; Schneider, J.; Willson, N.; Liu, J. C.; Mullen, C. Dept. of Neuropathology and Neurotoxicology, N.Y. State Psychiatric Institute, NY **Effects of prolonged LSD-25 administration upon neurons of spinal cord ganglia tissue cultures.** Journal of Neuropathology and Experimental Neurology. 33(2):212-225, 1974.

The effects of LSD-25 on spinal cord tissue is discussed. Rat spinal cord ganglia cultures were maintained for periods of up to 19 days in a feeding solution containing LSD-25 in a concentration of 5 micromoles. Electron microscopic examination of the nerve cells in these cultures revealed alterations in the Golgi complexes, lysosomes, mitochondria and multivesicular bodies. The changes in the membranous components of these structures were particularly prominent and resulted in organelle pleomorphism and very unusual internal membrane patterns. Variations were also noted in the fine structure of the nucleoli of some neurons. The possible relationships of the morphologic changes to disturbances of neuronal metabolism are considered. 40 references. (Author abstract)

185264 Groves, Philip M.; Rebec, George V.; Segal, David S. Dept. of Psychology, University of Colorado, Boulder, CO **The action of D-amphetamine on spontaneous activity in the caudate nucleus and reticular formation of the rat.** Behavioral Biology. 11(1):33-47, 1974.

The effects and time course of action of D-amphetamine, injected i.p.,on the spontaneous activity of neurons in the caudate nucleus were studied in rats. D-amphetamine injection in paralyzed, locally anesthetized rats, resulted in a biphasic alteration in spontaneous activity in the caudate nucleus. An initial dose dependent potentiation of activity occurs 5-10 min after injection followed by a prolonged dose dependent depression of activity. Similar injections result in a different time course of alterations in the mesencephalic reticular formation. Spontaneous activity in the caudate nucleus was relatively unaffected by mephentermine sulfate, a peripheral sympathomimetic. The depression of activity produced by amphetamine could be reversed by haloperidol. Haloperidol injected alone produced a transient potentiation of activity followed by a return to control firing rate. These results provide electrophysiological support for the inhibitory synaptic function of dopamine in the caudate-putamen and for the alleged action of amphetamine and haloperidol at these sites. Both the differential biochemical and neurophysiological effects of amphetamine on the caudate nucleus and reticular formation may have functionally significant behavioral consequences. 19 references. (Author abstract modified)

185582 Askew, William Earl. Univ. of Houston **Neurochemical role of adenosine 3',5'-cyclic monophosphate and guanosine 3',5'-cyclic monophosphate and their relation to neurotransmitters; effect of tetrahydrocannabinols. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-Films, No. 74-11837 HC$10.00 MF$4.00 99 p.

The neurochemical role of adenosine 3',5'-cyclic monophosphate (cAMP) and guanosine 3',5'-cyclic monophosphate (cGMP) and their relation to neurotransmitters were investigated. The effect of tetrahydrocannabinols is also studied. It was found that both delta8-THC and delta9-THC deplete whole rat brain acetylcholine levels whereas delta8-11-OH-THC has no significant effect. Delta8-THC has no effect on choline acetyltransferase activity but does decrease AchE activity. Acetylcholine content of rat brain synaptosomal preparations was significantly decreased. Dibutyryl cyclic AMP significantly increased locomotor activity in cannulated rats. Decreases in whole brain dopamine and norepinephrine levels were observed as well as an increase in serotonin and acetylcholine. Distribution of H3 dibutyryl cyclic AMP was primarily confined to the rat kidney and liver. Intraventricular injections of dibutyryl cyclic GMP had no effect on whole brain dopamine, norepinephrine, and serotonin levels while decreasing acetylcholine content in rat brain subcortical areas. Activity of dibutyryl cyclic GMP was also observed. (Journal abstract modified)

185725 Richards, Daniel Webster, III. Univ. of Houston **The general locus of d-amphetamine-induced discriminative stimuli. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-Films, No. 74-11826 HC$10.00 MF$4.00 100 p.

The general locus of d-amphetamine discriminative stimuli is investigated using two separate approaches involving intraventricular drug infusion; procedures of each approach are described. Results of both approaches demonstrate that intraventricular administrations of d-amphetamine are capable of producing a stimulus state that can acquire discriminative control of lever choice behavior in the rat. Neither intraventricular nor systemic injections of p-OH amphetamine are capable of producing a stimulus condition similar to that produced by either i.p. or intraventricular administrations of d-amphetamine. Findings indicate that the discriminative properties of d-amphetamine are mediated by the drug's direct actions upon the neurons of the central rather than peripheral nervous system. (Journal abstract modified)

185750 Sayers, A. C.; Handley, Sheila L. Research Institute Wander, CH-3001 Berne, Switzerland **Catalepsy induced by alpha-methyl-p-tyrosine and d-amphetamine: the role of catecholamine metabolism.** Psychopharmacologia (Berlin). 34(4):325-334, 1974.

The effect of inhibition of monamine oxidase, catechol-O-methyltransferase and Dopa-decarboxylase on the catalepsy induced by d-amphetamine in alpha-methyl-p-tyrosine treated rats was investigated. It was concluded that neither deaminated nor O-methylated products are responsible for the development of catalepsy. In fact, the indication was that the catalepsy may be antagonized by an O-methylated derivative.

A possible explanation for the action of the Dopa decarboxylase inhibitor is discussed. 26 references. (Author abstract modified)

185751 Castellano, C.; Eleftheriou, B. E.; Bailey, D. W.; Oliverio, A. Laboratorio di Psicobiologia e Psicofarmacologia C.N.R., Via Reno 1, 00198, Rome, Italy **Chlorpromazine and avoidance: a genetic analysis.** Psychopharmacologia (Berlin). 34(4):309-316, 1974.

A study was made to obtain a genetic analysis of the action of chlorpromazine on acquired avoidance behavior of mice in the shuttle box. Chlorpromazine was found to exert a significantly higher impairment on the performance of C57BL/6By than on BALB/cBy inbred mice pretrained in an active avoidance task. The effects of the drug on this measure assessed in these two strains, their reciprocal F1 congenic lines indicate that at least two genes modulate the action of chlorpromazine on avoidance behavior. It was possible to characterize one of the loci modulating the effect of chlorpromazine on avoidance performance, and the symbol Cpz was assigned to it. The locus is in chromosome 9, linkage group II. 10 references. (Author abstract modified)

185866 Soyka, Lester F.; Deckert, Fred W. Dept. of Pharmacology, University of Vermont, College of Medicine, Burlington, VT 05401 **Further studies on the inhibition of drug metabolism by pregnanolone and related steroids.** Biochemical Pharmacology (Oxford). 23(11):1629-1639, 1974.

A variety of other steroids and naturally occurring substances were tested for inhibition of the O-demethylation of p-nitroanisole by 9000g hepatic supernatants from adult male rats, because of previous findings that pregnanolone and related metabolites of progesterone inhibit drug demethylation and hydroxylation reactions in vitro. Of some 58 steroids tested, none was more potent than pregnanolone. Inhibitory activity was not related to the endocrine activity of the steroid. Inhibition by a group of 11 steroids was generally greater with 9000g supernatants from female rats, and was uniformly increased with supernatants from pregnant rats. By 10 days after delivery, inhibition returned to levels equivalent to those found with supernatants from virgin females. Cholesterol and related compounds, fatty acids and esters, ceramides, gangliosides, phosphatidyl inositol and other natural fatty acid conjugates and a variety of indoles and lipids had no inhibitory activity. Pregnanolone administration increased the duration of hexobarbital and of barbital induced sleep in rats, apparently due to an additive sedative effect. However, microsomes prepared from these animals exhibited lesser rates of demethylation, with kinetics compatible with uncompetitive inhibition. Results indicate that progesterone, its metabolites and structurally similar steroids are potent inhibitors of microsomal drug metabolism. It is felt that such inhibition may be responsible, in part, for the low rates of drug metabolism seen in the female during pregnancy, and in the neonate. 15 references. (Author abstract modified)

185899 Engel, Jorgen; Lundborg, Per. Dept. of Pharmacology, Univ. of Goteborg, Fack, S-400 33 Goteborg 33, Sweden **Regional changes in monoamine levels and in the rate of tyrosine and tryptophan hydroxylation in 4 week old offspring of nursing mothers treated with the neuroleptic drug penfluridol.** Archives of Pharmacology (Berlin). 282(4):327-334, 1974.

Regional changes in the monamine levels and in the rate of tyrosine and tryptophan hrdroxylation in the offspring of nursing rat mothers treated with penfluridol were examined. The rat mothers were given penfluridol on days one, three and five after delivery. The male litter mates were killed 4 weeks after birth 30 min after treatment with an inhibitor of aromatic l-aminoacid-decarboxylase (NSD-1015) and the concentrations of noradrenaline, dopamine and 5-hydroxytryptamine were analyzed in regional brain areas. The accumulation of Dopa and 5-hydroxytryptophan after the administration of NSD-1015 was analyzed. In the offspring of mothers treated with penfluridol a marked decrease in the rate of tyrosine hydroxylation in specific brain regions was observed. The possibility that penfluridol interacts with the development of monoaminergic mechanisms in the brain at a sensitive developmental period and therby induces a decreased functional activity in central monoamine neurones especially in the limbic system is discussed. 27 references. (Author abstract modified)

185900 Konermann, G.; Streffer, C. Institut fur Biophysik und Strahlenbiologie, Universitat Freiburg, D-7800 Freiburg i Br., Albertstrasse 23, Germany **Histo-autoradiographic investigations on the distribution of injected 5-hydroxytryptamine (serotonin) in the brain and the pituitary of mice.** Archives of Pharmacology (Berlin). 282(4):349-365, 1974.

The distribution of 5-hydroxytryptamine (5-HT) was investigated by histoautoradiography in the mouse brain after intraperitoneal and intracerebral injection under conditions which are optimal for the radioprotective effect of the amine. As early as three min after i.p. injection extensive labelling was observed in hypothalamic brain regions, in the infundibulum and all parts of the pituitary. The maximal radioactivity was reached in the pituitary at a later period than in the infundibulum. An anatomically differentiated distribution was observed with lower radioactivity in all other brain regions. After intracerebral injection the distribution of 5-HT was rapid. No difference was observed for either hemisphere during the period investigated (3 to 30 min). The hippocampus formation and the marginal zones of the whole ventricle system were labeled most intensively. All brain regions showed a maximum of radioactivity 6 min after the injection. The time course of the labelling in the brain and of the radioprotective effect by 5-HT show a similarity. 49 references. (Author abstract modified)

185901 Grossmann, W.; Jurna, I.; Theres, C. Institut fur Pharmakologie und Toxikologie der Univ. d. Saarlandes, D-6650 Homburg (Saar), Germany **The site of action on the optical isomers of 1-methyl-5-phenyl-5-propyl barbituric acid.** Archives of Pharmacology (Berlin). 282(4):367-377, 1974.

The effects of the optical isomers of 1-methyl-5-phenyl-5-propyl barbituric acid (MPPB) on spinal reflexes and on single motoneurons was studied in spinal rats after i.v. adminstration. The amplitudes of monosynaptic and polysynaptic reflexes in the rat were reduced by (-)-MPPB and increased by (+)-MPPB. (-)-MPPB increased the membrane resistance and the firing level of cat motoneurons and reduced the amplitude of monosynaptic excitatory postsynaptic potentials. (+)-MPPB lowered the membrane resistance and the firing level of the motoneurons and increased the monosynaptic excitatory postsynaptic potentials. Both isomers did not significantly influence the resting potential and the action potentials elicited by antidromic stimulation. It was concluded that the two isomers of MPPB in the doses employed act on postsynaptic and presynaptic sites and produce their opposite effects (depression or excitation) by an action on the same neuronal membranes. 17 references.

185902 Philippu, A.; Demmeler, R.; Roensberg, G. Institut f. Pharmakologie und Toxikologie der Univ. Wurzburg, D-8700

Wurzburg, Koellikerstr. 2, Germany **Effects of centrally applied drugs on pressor responses to hypothalamic stimulation.** Archives of Pharmacology (Berlin). 282(4):389-400, 1974.

The effects of centrally applied drugs on pressor responses to hypothalamic stimulation was investigated in the cat. The posterior hypothalamus of anesthetized cats was superfused through a push pull cannula with artifical cerebrospinal fluid and electrically stimulated with the noninsulated tip of the cannula. The hypothalamus was superfused with drugs and their effects on the pressor responses to hypothalamic stimulation were studied. The effects of superfusion with concentrations of clonidine, carbachol and hexamethonium are noted. Results suggest that: low concentrations of clonidine enhance the pressor responses to hypothalamic stimulation by activating the alpha-adrenoceptors of the hypothalamic area; high concentrations inhibit the pressor responses: nicotine agents enhance the rise of blood pressure caused by hypothalamic stimulation: and more than one neurotransmitter seems to be involved in the central modulation of the arterial blood pressure. 17 references. (Author abstract modified)

185931 Magour, S.; Coper, H.; Fahndrich, Ch. Institut fur Neuropsychopharmakologie der Freien Universitat Berlin, D-1000 Berlin 19, Ulmenalle 30, Germany **The effects of chronic treatment with d-amphetamine on food intake, body weight, locomotor activity and subcellular distribution of the drug in rat brain.** Psychopharmacologia (Berlin). 34(1):45-54, 1974.

The effects of chronic treatment with d-amphetamine on the food intake, body weight, locomotor activity and subcellular distribution of the drug in the brains of rats was examined. Female rats were treated chronically with amphetamine sulphate and the consumed doses increased from 16mg/kg on the first day to 90mg/kg on the 36th day. The rats developed tolerance to the overall toxicity and to the anorexigenic effect of amphetamine. No tolerance to the effects of the drug on body weight and locomotor activity was observed. The concentration of H3-d-amphetamine in brains of chronically treated rats was significantly higher than in controls. No difference in the pattern of distribution of radioactivity among the subcellular fractions of rat brain was observed between control and treated groups. The relationship between development of tolerance and the concentration of amphetamine in the brain is discussed. (Author abstract modified)

185933 Bite, Agnes; Gyorgy, L. Institute of Experimental Medicine, Hungarian Academy of Sciences, 1450 Budapest 9, POB 67, Hungary **Studies on the potentiation of the antinociceptive effect of oxotremorine by tetrabenazine in mice.** Psychopharmacologia (Berlin). 34(1):63-70, 1974.

The potentiation of the antinociceptive effect of oxotremorine by tetrabenazine was studied in mice. The antinociceptive effect of oxotremorine in mice was increased by tetrabenazine in the hot plate test. This effect was antagonized by desmethylimipramine and amphetamine and enhanced by 5-hydroxytryptophan. Pretreatment with tetrabenazine prevented the increase in the level of acetycholine in the brain induced by oxotremorine. There was no correlation between the antinociceptive effect and the acetylcholine concentration in the brain in animals treated with oxotremorine. It was suggested that in the enhancement of the antinociceptive effect of oxotremorine caused by tetrabenazine, the depletion of catecholamines and not that of serotonin plays a predominant role. 15 references. (Author abstract)

185992 Ortiz, Aurelio; Griffiths, Peter J.; Littleton, John M. Dept. of Pharmacology, Kings College, Strand, London WC2, England **A comparison of the effects of chronic administration of ethanol and acetaldehyde to mice: evidence for a role of acetaldehyde in ethanol dependence.** Journal of Pharmacy and Pharmacology (London). 26(4):249-260, 1974.

The effects of chronic administration of ethanol and acetaldehyde to mice are compared. After chronic exposure to ethanol or acetaldehyde vapour in concentrations which depress locomotor activity, mice show similar behavioral changes during withdrawal, and there is some degree of cross dependence. Mice exposed to acetaldehyde vapour had blood acetaldehyde concentrations similar to those of ethanol treated mice, but brain acetaldehyde concentrations were apparently lower. There was no accumulation of acetaldehyde in blood or brain in either group during chronic administration. Chronic ethanol or acetaldehyde administration to mice is associated with an increase in the concentrations of the brain monoamines noradrenaline, dopamine and 5-HT. Withdrawal of ethanol or acetaldehyde is associated with a further, rapid, transient rise in the brain catecholamines, noradrenaline and dopamine. These results suggest that acetaldehyde may play a role in some of the biochemical and behavioral changes associated with ethanol dependence. 21 references. (Author abstract)

185993 Bonilla, Ernesto; Diez-Ewald, Maria; Medrano, Jose Finol. Instituto de Investigacion Clinica, Facultad de Medicina, Universidad del Zulia, Maracaibo, Venezuela **Effect of L-dopa in 54 Mn incorporation by tissues.** Journal of Pharmacy and Pharmacology (London). 26(4):261-264, 1974.

Mn incorporation by tissues was studied in 24 rats fed with excess manganese diet and 31 fed a normal diet. The effect of intraperitoneally administered L-dopa on randomly selected rats in each group was determined. Manganese uptake in liver was higher in normally fed rats that received L-dopa; however, the manganese loaded rats showed a lower level of 54 Mn incorporation than those on a normal diet. No difference in 54 Mn incorporation was found in submaxillary glands from any of the groups studied. In brain tissue, 2 h after injection of L-dopa, the 54 Mn radioactivity was the same in normal and manganese loaded animals and significantly higher than in rats not given the amine. The reverse effect was found in serum which from L-dopa-treated rats showed lower radioactivity than the controls, suggesting an increased passage of the tracer to the tissues. It is felt that the different response of tissues from manganese loaded rats could mean that the enzyme adenyl cyclase may be affected by the excess of manganese. Since dopamine does not cross the blood brain barrier, the L-dopa increase of 54 Mn uptake by brain could occur in the endothelial cells of the capillaries. 9 references. (Author abstract)

185995 Consolo, S.; Ladinsky, H.; Garattini, S. Istituto di Richerche Farmacologiche, 'Mario Negri', Via Eritrea 62, Milan, Italy 20157 **Effect of several dopaminergic drugs and trihexyphenidyl on cholinergic parameters in the rat striatum.** Journal of Pharmacy and Pharmacology (London). 26(4):275-277, 1974.

The effect of several direct and indirect acting dopamine like drugs, as well as the antimuscarinic agent trihexyphenidyl, on some cholinergic parameters in the striatum was examined in female Sprague-Dawley rat brain homogenates to explore the possibility that a cholinergic mechanism may be involved in some symptoms of parkinsonism. The dopamine like drugs included L-dopa, 1-(2'-pyrimidyl)-4-piperonyl-piperazine (piribedil), amantadine HCl, desipramine, and (+)-amphetamine sulphate. The time courses and dose response effects of these drugs on striatal acetylcholine and choline levels

are shown. All drugs save for trihexyphenidyl increased striatal acetylcholine levels. Choline levels were unaffected by L-dopa, amphetamine, and desipramine while they were increased by amantadine, apomorphine, and piribedil. Trihexyphenidyl did not affect choline levels. It is suggested that the drugs act indirectly by blocking the release of acetylcholine. Furthermore, the data indicate that the dopamine pathway modulates the action of cholinergic neurons by inhibitory input. The findings with trihexyphenidyl support this view. 20 references.

185996 Gardey-Levassort, C.; Lechat, P. Institut de Pharmacologie, 21, rue de l'Ecole-de-Medecine, 75270 Paris Cedex 06, France **Dose-dependent potentiation or inhibition by Ro4-4602 of 5-HTP hyperthermia in rabbits.** Journal of Pharmacy and Pharmacology (London). 26(4):278-279, 1974.

The dose dependent potentiation or inhibition by Ro4-4602, a dopa-5-HTP decarboxylase inhibitor, of 5-HTP hyperthermia in rabbits was investigated. With the lowest dose of Ro4-4602 tested, all the rabbits exhibited a potentiation of the hyperthermic effect of 5-HTP, and death ensued in less than 210 min. The highest dose of Ro-4602 resulted in total inhibition of the hyperthermia produced by 5-HTP, followed 60 to 75 min after injection of the 5-HTP by hypothermia. The injection of Ro-4602 alone had no effect on temperature. It is suggested that at the lowest dose, Ro4-4602 inhibits mainly the peripheral decarboxylases, allowing an increased amount of 5-HTP to reach the brain where it is decarboxylated, liberating a large quantity of 5-HT. The decreasing mortality and hyperthermia noted with increased doses of Ro4-4602 may be attributable to intracerebral penetration of the inhibitor at these dose levels, resulting in a decreased cerebral metabolism of 5-HTP, and no increase in levels of cerebral 5-HT. The hypothermia observed after administration of the highest dose of Ro4-4602 followed by 5-HTP may result from the hypothermic action of low doses of 5-HT. Possible involvement by dopamine is discussed. 13 references.

186033 Toran-Allerand, C. Dominique. Dept. of Neurology, Columbia Univ. College of Physicians and Surgeons, New York, NY 10032 **Acetylcholinesterase inhibition and myelinogenesis in vitro.** Experimental Neurology. 43(1):216-226, 1974.

A long acting, reversible acetylcholinesterase inhibitor, ambenonium chloride (Mytelase), was added to developing cultures of neonatal mouse cerebellum to study its effect on myelin sheath formation. Myelinogenesis was inhibited completely in some cultures, retarded in others or apparently unaffected. The numbers of myelin sheaths per culture were also significantly reduced. Withdrawal of the compound resulted in the (re)initiation of myelinogenesis after 48 hr. The pattern of inhibition suggests that the acetylcholinesterase containing neurons are the ones affected and supports the concept that the neuron may play an active role in the myelinogenetic process. 18 references. (Author abstract)

186375 Graham, D. T.; Erickson, C. K. Dept. of Pharmacology, School of Pharmacy, University of Kansas, Lawrence, KS **Alteration of ethanol-induced CNS depression: ineffectiveness of drugs that modify cholinergic transmission.** Psychopharmacologia (Berlin). 34(2):173-180, 1974.

The relevance of reduced acetylcholine (ACh) release to the central depressant effect of ethanol was studied in rats trained to perform in a discriminated lever press avoidance situation. Rats were given ethanol orally to depress their performance. In an attempt to modify the ethanol induced depression with drugs which would reverse or enhance reported effects of ethanol in reducing free cerebral ACh, parenteral atropine, intraventricular hemicholinium, and intraventricular ACh were given during ethanol intoxication. None of the drugs significantly altered the ethanol induced behavioral depression, suggesting that the reported reduction in free ACh during ethanol intoxication may reflect decreased neuronal activity rather than causing ethanol induced central nervous system depression. 11 references. (Author abstract modified)

186569 Kohli, R. P.; Singh, N.; Kulshrestha, V. K. Department of Pharmacology and Therapeutics, King George's Medical College, Lucknow 226003, India **An experimental investigation of dependence liability of methaqualone in rats.** Psychopharmacologia (Berlin). 35(4):327-334, 1974.

The dependence liability of methaqualone was examined in rats. Ss were kept on a semifluid diet, and methaqualone and phenobarbitone were added to the diet of different groups of animals. Every week the doses of the drugs were increased and daily records of body weight, mean rectal temperature and spontaneous motor activity were maintained. Tolerance to both the drugs was discernible in the first and second week. In the third week the doses were increased and at the end of this week although there was gradual and partial recovery, statistically significant lowering of mean rectal temperature, body weight and spontaneous motor activity was observed in comparison to a control group of rats. After the third week when the drugs were withdrawn from the diet methaqualone treated rats exhibited increased susceptibility to audiogenic stimuli. Rats similarly treated with phenobarbitone showed a greater susceptibility to audiogenic stimuli, and in addition exhibited increased motor activity and a precipitous decrease in body weight. The results of this study are suggestive of a milder degree of dependence liability in methaqualone as compared with barbiturates. 13 references. (Author abstract)

186570 Abel, E. L.; Cooper, C. W.; Harris, L. S. Research Institute on Alcoholism, 1021 Main Street, Buffalo, NY 14203 **Effects of delta9-tetrahydrocannabinol on body weight and brain electrolytes in the chicken.** Psychopharmacologia (Berlin). 35(4):335-339, 1974.

The effects of delta9-tetrahydrocannabinol (THC) on body weight and brain electrolytes were examined in the chicken. Baby chicks were administered daily injections of THC and records were kept of their body weight. The drug produced a marked decrease in weight gain. At 3 weeks old, these animals were sacrificed and the concentration of various electrolytes in their brains was determined, along with another group of drug naive animals. There were no differences in electrolyte concentrations for the chronically treated animals, but sodium and potassium levels were markedly increased in the acute group. 8 references. (Author abstract)

186575 Izquierdo, Ivan. Departamento de Fisiologia, Farmacologia e Biofisica, Instituto de Biociencias, U.F.R.G.S., Caixa Postal No. 592, 90000 Porto Alegre, Brazil **Possible peripheral adrenergic and cholinergic mechanisms in pseudoconditioning.** Psychopharmacologia (Berlin). 35(3):189-193, 1974.

In a study of peripheral adrenergic and cholinergic mechanisms in pseudoconditioning, buzzers and shocks were presented in random sequence and with no temporal association to rats in a shuttle box, so that they performed pseudoconditioned barrier crossing responses to the buzzer. Performance of these responses was enhanced by amphetamine and tyramine. The adrenergic blocking agents yohimbine and dibenamine, though ineffective on their own, antagonized the

action of amphetamine and tyramine. Hexamethonium and methylatropine, also ineffective by themselves, potentiated the effect of amphetamine but not that of tyramine. Eserine depressed the performance of pseudoconditioned responses when given alone, and it antagonized the stimulant action of both amphetamine and tyramine. The results suggest that amphetamine and tyramine enhance pseudoconditioning through activation of a peripheral adrenergic mechanism and that amphetamine, in addition, triggers an opposing cholinergic mechanism, also peripheral, from which it can be released by the anticholinergic agents hexamethonium and methylatropine. The depressant action of eserine can also be explained by activation of the cholinergic mechanism. 14 references. (Author abstract)

186577 Costall, B.; Naylor, R. J. Postgraduate School of Studies in Pharmacology, University of Bradford, Bradford, Yorkshire, England **A role for the amygdala in the development of the cataleptic and stereotypic actions of the narcotic agonists and antagonists in the rat.** Psychopharmacologia (Berlin). 35(3):203-213, 1974.

The electrolytic brain lesion technique was used to assess the role of the nucleus amygdaloideus centralis in the mediation of the catalepsy and stereotyped behavior induced in the rat by the narcotic agonists and antagonists. M6029 and M6007 exhibited a biphasic action in the rat consisting initially of catalepsy induction followed by the development of stereotyped gnawing, biting and licking responses with a transition period when both behaviors were apparent. Morphine and M320 produced a cataleptic response in the rat but stereotyped behavior did not develop. Bilateral ablation of the nucleus amygdaloideus centralis was found to abolish the cataleptic phase of the effects of M6029 and M6007 and to markedly enhance the stereotypic phase. The lesions were similarly shown to markedly reduce or abolish the cataleptic effects of morphine and M320 and, in contrast to the actions of these drugs in normal animals, a periodic stereotyped behavior developed. A role is suggested for the nucleus amygdaloideus centralis in the genesis of the cataleptic action of the narcotic agonists and antagonists. An amygdaloid - cataleptic: striatal - stereotypic balance is hypothesized for the action of these agents in the rat. 21 references. (Author abstract)

186578 Lahti, Robert A.; Barsuhn, Craig. CNS Diseases Research, Upjohn Company, Kalamazoo, MI 49001 **The effect of minor tranquilizers on stress-induced increases in rat plasma corticosteroids.** Psychopharmacologia (Berlin). 35(3):215-220, 1974.

A variety of psychoactive drugs were evaluated for their ability to block a stress induced elevation in rat plasma corticosteroids. Stress was applied by placing the rats in different cages and moving them to a novel environment which resulted in a rapid increase in plasma corticosteroids, near maximal with 30 min, followed by a decrease to normal by 2 h. Meprobamate, phenobarbital, diazepam and several other benzodiazepines, all of which exhibit anxiolytic properties, were able to block the stress induced increase. U-33,030 and U-31,889, two triazolobenzodiazepine derivatives, were the most potent compounds tested. No other type of psychoactive compound demonstrated this activity. 7 references. (Author abstract)

186579 Saarnivaara, Liala; Mattila, M. J. Department of Pharmacology, University of Helsinki, Siltavuorenpenger 10 SF-00170 Helsinki 10, Finland **Comparison of tricyclic antidepressants in rabbits: antinociception and potentiation of the noradrenalin pressor responses.** Psychopharmacologia (Berlin). 35(3):221-236, 1974.

The antinociceptive effect on the rabbit's dental pain of 10 tricyclic antidepressants was compared with their potentiation of the noradrenaline (NA) pressor responses in conscious rabbits. The receptor desensitization by tricyclic antidepressants was tested on the rabbit's isolated aortic spiral. Tertiary amines imipramine, amitriptyline, doxepine, and trimipramine were most antinociceptive but inferior to morphine. They were also most potent in enhancing the morphine analgesia, amitriptyline and doxepine in particular. The secondary amines desipramine and nortriptyline were less antinociceptive than their tertiary analogs imipramine and amitriptyline. Lithium abolished the antinociceptive action of protriptyline without modifying that of the combination of protriptyline and morphine. The secondary amines, protriptyline and nortriptyline, proved most effective in enhancing the NA pressor response, followed by dibenzepine, desipramine, and imipramine. Opipramol, amitriptyline and iprindole were least active. Trimipramine reduced the NA pressor responses and the effect of doxepine was variable. It is concluded that antinociception by tricyclic antidepressants is more likely related to their central tryptaminergic mechanisms or to local anaesthetic properties than to their adrenergic or adrenolytic activity. 38 references. (Author abstract)

186582 Baez, Luis A. Department of Psychology, Princeton University, Princeton, NJ 08540 **Role of catecholamines in the anorectic effects of amphetamine in rats.** Psychopharmacologia (Berlin). 35(2):91-98, 1974.

The role of catecholamines in the anorectic effects of amphetamines in rats was studied. The inhibition of catecholamine synthesis with alpha-methyl-p-tyrosine antagonized amphetamine induced anorexia. This effect of alpha-methyl-p-tyrosine was reversed by L-dopa administration. Comparison of the anorectic potencies of the stereoisomers of amphetamine yielded a d-amphetamine to l-amphetamine ratio of 2.75:1. It is concluded that amphetamine produces anorexia through an action on catecholamines, with dopamine playing a major role. 31 references. (Author abstract)

186585 Kaymakcalan, Sukru; Turker, R. Kazim; Turker, Mustafa N. Department of Pharmacology, Ankara University, Medical School, Sihhiye/Ankara, Turkey **Analgesic effect of delta9-tetrahydrocannabinol in the dog.** Psychopharmacologia (Berlin). 35(2):123-128, 1974.

Evidence is presented that in the electrical stimulation of the tooth of the dog delta9-tetrahydrocannabinol (THC) (1 mg/kg) produced analgesia. Daily administrations caused tolerance to this effect in 8 days. The nature of the analgesia induced by THC is discussed. 13 references. (Author abstract)

186632 Joy, R. M.; Edmonds, H. L. Department of Physiological Sciences, School of Veterinary Medicine, University of California, Davis, CA 95616 **The antagonism of hippocampal and cortical afterdischarge by SC-13504, a new anticonvulsant.** Neuropharmacology (Oxford). 13(3):145-157, 1974.

The antagonism of hippocampal and cortical afterdischarge by SC-13504 a new anticonvulsant in cats is described. SC-13504 is more active and potent than either diphenylhydantoin or phenobarbital in antagonizing afterdischarges produced by cortical or hippocampal stimulation. It is capable of abolishing afterdischarges at doses at or below those producing minimal behavioral alterations in chronic cats. Changes observed in behavior, electroencephalograms, and on thresholds for

arousal and recruiting demonstrate that in these regards SC-13504 is more similar to known tranquilizing agents than to sedative hypnotics. SC-13504 may be considered structurally as either a diphenylmethane derivative or as a hydrazone derivative. Because of its unique structure as compared to the majority of anticonvulsants and because of its marked anticonvulsant properties, further evaluation is indicated. 33 references. (Author abstract)

186633 Komiskey, H.; Buckner, C. K. School of Pharmacy, University of Wisconsin, Madison, WI 53706 **Effects of lithium on adrenergic amine uptake in rat brain synaptosomes.** Neuropharmacology (Oxford). 13(3):159-164, 1974.

The effects of lithium on the uptake and retention of (-)-erythro-metaraminol (MA) and (-)-m-octopamine (OA) by synaptosomes from rat whole brain were examined after addition of lithium chloride to synaptosomal fractions in vitro and administration of lithium chloride to rats twice daily for 10 days prior to isolation of synaptosomes. Under control conditions, apparent Km concentrations (5 min incubation) for MA and OA were 33 and 3 micromoles respectively. As incubation times were increased to 15 min, retention of MA increased and OA decreased. Retention of both amines was reduced by low temperature. Short-term application of lithium to synaptosomes in vitro did not alter the uptake and retention of either amine during 5 or 10 min incubation periods. Chronic pretreatment of rats with lithium resulted in greater uptake and retention of low concentrations of MA when compared with synaptosomes from control (saline treated) animals. Chronic lithium pretreatment did not alter retention of OA. The data support the hypothesis that lithium acts to increase synaptosomal membrane uptake of aromatic amines and decrease binding of accumulated amine. 20 references. (Author abstract)

186640 Beleslin, D. B.; Dimitrijevic, M.; Samardzic, Ranka. Department of Pharmacology, School of Veterinary Medicine, Beograd 11 105, Yugoslavia **Hyperthermic effect of palmitate sodium, stearate sodium and oleate sodium injected into the cerebral ventricles of conscious cats.** Neuropharmacology (Oxford). 13(3):221-223, 1974.

The hyperthermic effect of palmitate sodium, stearate sodium and oleate sodium injected into the cerebral ventricles of conscious cats is reported. Threshold effects were obtained with as little as 20-50 micrograms of palmitate sodium and stearate sodium or 20.0micrograms of oleate sodium. The hyperthermic effect of these fatty acids reached its maximum 2-3 hr after administration and lasted for more than 12 hr. The rise in temperature was always associated with sedation. The temperature was not affected by an i.p. injection of palmitate sodium, stearate sodium or oleate sodium. 11 references.

186665 Martin, W. R.; Eades, C. G.; Thompson, W. O.; Thompson, J. A.; Flanary, H. G. NIDA Addiction Research Center, P.O. Box 2000, Lexington, KY 40507 **Morphine physical dependence in the dog.** Journal of Pharmacology and Experimental Therapeutics. 189(3):759-771, 1974.

A procedure for making chronic spinal dogs physically dependent on morphine and maintaining them for many months is described. The qualitative characteristics of the precipitated abstinence syndrome appear to depend on the level of dependence, whereas the withdrawal abstinence syndrome does not. The dependent spinal dog was used to assay the relative potencies of antagonists in precipitating abstinence. Morphine suppresses the withdrawal abstinence syndrome in a dose related manner. Haloperidol was found to suppress certain signs of abstinence, but not others. Propranolol was found to suppress certain signs of abstinence, but not others. Propranolol neither suppressed nor precipitated abstinence. The primary abstinence syndrome, characterized by increased pulse rate, pupillary diameter, respiratory rate and responsivity to nociceptive stimuli, became maximal on the 2nd day of withdrawal abstinence and persisted for about 1 week. A protracted syndrome then emerged characterized by a decrease in body temperature, slowing of pulse rate and respiratory rate, shortening of the latency of the skin twitch reflex, decreased responsivity of the flexor reflex to a low level of noxious stimuli and increased responsivity to medium and high strengths of stimuli. The relationship between these findings and exacerbation of the psychopathic personality as a consequence of narcotic addiction is discussed. 26 references (Author abstract modified)

186666 Boyd, Eugene S.; Boyd, Eleanor H.; Brown, Lawrence E. University of Rochester, School of Medicine and Dentistry, 260 Crittenden Blvd., Rochester, NY 14642 **The effects of some drugs on an evoked response sensitive to tetrahydrocannabinols.** Journal of Pharmacology and Experimental Therapeutics. 189(3):748-758, 1974.

The effects of several drugs were compared with those of delta9-tetrahydrocannabinol (THC) on responses evoked in frontal lobe polysensory areas, ipsilateral and contralateral to the stimulus site in primary somatosensory cortex, in squirrel monkeys with postmesencephalic or high spinal sections. THC augmented both the early evoked response and the late evoked response, which occurs 150 to 200 msec after the stimulus. Pentobarbital, ethanol and diethyl ether depressed both early and late responses, while chlorpromazine and chloralose depressed late responses without consistently affecting early responses; none of these drugs induced late repetitive activity. Mescaline had effects similar to those of THC on late responses, but its effect on early responses was much less. Lysergic acid diethylamide had little effect on early responses but depressed late responses at high doses. Phencyclidine also had little effect on early responses. It facilitated late responses at low doses and depressed them at high doses. Picrotoxin and pentylenetetrazol had effects similar to, but greater than those of THC. 23 references. (Author abstract modified)

186668 Yang, H. -Y. T.; Neff, N. H. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **The monoamine oxidases of brain: selective inhibition with drugs and the consequences for the metabolism of the biogenic amines.** Journal of Pharmacology and Experimental Therapeutics. 189(3):733-740, 1974.

Two types of monoamine oxidase were identified in vivo in rat brain. These enzymes, designated as type A and type B, were inhibited differentially by the drugs clorgyline (inhibitor of type A enzyme) and deprenyl (inhibitor of type B enzyme). It is suggested that the two types of enzyme are responsible for the metabolism of different amines in vivo and that the metabolism of the amines can be altered selectively by administration of these drugs. Norepinephrine and serotonin were preferred substrates for type A enzyme and injection of clorgyline induced an elevation of these amines in brain. Beta-Phenylethylamine was preferred substrate for type B enzyme and injection of deprenyl slowed the metabolism of beta-phenylethylamine in brain. In contrast to the aforementioned amines, dopamine was a substrate for both enzymes and injection of either drug resulted in elevated dopamine concentrations. It is concluded that it may be possible to alter selectively the metabolism of the putative transmitter amines in man by administration of monoamine oxidase inhibitor drugs that

preferentially inactivate a specific type of monoamine oxidase. 23 references. (Author abstract)

186669 Wenger, Galen R.; Rutledge, Charles O. Laboratory of Psychobiology, Harvard Medical School, 25 Shattuck St., Boston, MA 02115 **A Comparison of the effects of amphetamine and its metabolites, p-hydroxyamphetamine and p-hydroxynorephedrine, on uptake, release and catabolism of 3H-norepinephrine in cerebral cortex of rat brain.** Journal of Pharmacology and Experimental Therapeutics. 189(3):725-732, 1974.

The effects of amphetamine and its metabolites, p-hydroxyamphetamine and p-hydroxynorephedrine on uptake, release and catabolism of 3H-norepinephrine were compared in cerebral cortex of rat brain. Amphetamine, p-hydroxyamphetamine and p-hydroxynorephedrine inhibited the uptake of 3H-norepinephrine into chopped cerebral cortex in vitro. Although all three substances were capable of producing 100% inhibition of uptake, amphetamine and p-hydroxyamphetamine were more potent than p-hydroxynorephedrine. When cerebral cortex was incubated with 3H-norepinephrine prior to the addition of the drug, all three drugs caused a concentration related release of 3H-norepinephrine into the incubation medium. p-Hydroxynorephedrine was less potent than amphetamine and p-hydroxyamphetamine. p-Hydroxynorephedrine also produced a small but significant elevation in the proportion of 3H-deaminated metabolites of 3H-norepinephrine in the release experiments, while amphetamine and p-hydroxyamphetamine caused a concentration related decrease in 3H-deaminated metabolites. In homogenates of cerebral cortex, amphetamine and p-hydroxyamphetamine produced significant inhibition of monoamine oxidase. These results suggest that, in addition to releasing 3H-norepinephrine into the medium, p-hydroxynorephedrine also displaced 3H-norepinephrine. 37 references. (Author abstract modified)

186671 Tseng, L. F.; Hitzemann, R. J.; Loh, H. H. Department of Pharmacology, University of California Medical Center, San Francisco, CA 94143 **Comparative effects of dl-p-methoxyamphetamine and d-amphetamine on catecholamine release and reuptake in vitro.** Journal of Pharmacology and Experimental Therapeutics. 189(3):708-716, 1974.

In an investigation of the different behavior effects caused by dl-p-methoxyamphetamine (PMA) and d-amphetamine, a comparison was made between the effects of the two drugs on the release and reuptake of 3H-norepinephrine (NE) and 3H-dopamine (DA) in tissue slices prepared from the cerebral cortex and the corpus striatum of the rat brain. PMA was found to be equipotent to d-amphetamine in causing the release of 3H-NE from the cortex. PMA also increased the release of newly synthesized 3H-NE formed from 3H-DA in this region. However, PMA was less potent than d-amphetamine in causing the release of 3H-DA either taken up from the incubation medium or formed from 3H-tyrosine in the corpus striatum. PMA, like d-amphetamine, competitively blocks the reuptake of 3H-NE and of 3H-DA into slices prepared from the cortex and corpus striatum, respectively. PMA was 14% as effective as d-amphetamine in blocking 3H-DA uptake in the corpus striatum and was 29% as effective as d-amphetamine in blocking 3H-NE uptake in the cortex. The results suggest that the relatively weak effect of PMA on catecholamine release and reuptake in structures rich in DA containing neurons may be related to the lack of effect of PMA on locomotor activity and stereotyped behaviors. 36 references. (Author abstract)

186672 Yeh, J. Z.; Narahashi, Toshio. Department of Physiology and Pharmacology, Duke University Medical Center, Durham, NC 27710 **Noncholinergic mechanism of action of cholinergic drugs on squid axon membranes.** Journal of Pharmacology and Experimental Therapeutics. 189(3):697-707, 1974.

The effects of acetylcholine and other cholinergic drugs on squid axon membranes were studied by means of internal perfusion and voltage clamp techniques in an attempt to characterize the nature of axonal cholinergic receptors. External application of carbamylcholine, decamethonium and d-tubocurarine had little or no effect on resting and action potentials. When perfused internally, acetylcholine, carbamylcholine, hexamethonium and decamethonium had no effect on the resting membrane potential whereas d-tubocurarine hyperpolarized the membrane by 4 mV. The amplitude of the action potential was slightly decreased and its duration prolonged, and peak transient and steady state conductances were slightly suppressed by internal perfusion of acetylcholine, carbamycholine and hexamethonium. Decamethonium decreased the height of the action potential to 70% of the control and prolonged its duration. It decreased the peak transient conductance to 50% of the control and left steady state conductance unchanged. d-Tubocurarine decreased the height of the action potential to 50% of the control and prolonged its duration remarkably. Both peak transient and steady state conductances were almost equally suppressed and the effect was concentration dependent. d-Tubocurarine also slowed the sodium inactivation process. 32 references. (Author abstract modified)

186673 Suria, Amin; Costa, E. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeths Hospital Hospital, Washington, DC 20032 **Diazepam inhibition of post-tetanic potentiation in bullfrog sympathetic ganglia: possible role of prostaglandins.** Journal of Pharmacology and Experimental Therapeutics. 189(3):690-696, 1974.

The role of prostaglandins in diazepam inhibition of post-tetanic potentiation (PTP) in bullfrog sympathetic ganglia was examined. PTP of the fast excitatory postsynaptic potential (EPSP) in the curare treated sympathetic ganglion of the bullfrog was inhibited by diazepam in a dose dependent manner. Prostaglandins (PGs) of the E series (PGE and PGE) mimicked the action of diazepam. Arachidonic acid also inhibited the PTP of EPSP. The inhibition obtained with diazepam could be potentiated in the presence of PGs of arachidonic acid. Pretreating the ganglion with 5,8,11,14-eicosatetraynoic acid, a prostaglandin synthetase blocker, abolished diazepam and arachidonic acid inhibition of PTP but not that of PGs. If the receptors for prostaglandins were blocked with a dibenzoxazepine derivative (SC 19220), the response to diazepam and arachidonic acid, as well as the PGs was abolished. None of these compounds inhibited the potential evoked by single shock. These data suggest that PGs may be involved in the action of diazepam in inhibiting the PTP. It is postulated that diazepam may increase the activity of PG synthetase that would result in the increased production of PGs, which may inhibit PTP of EPSP. 29 references. (Author abstract)

186674 Knapp, Suzanne; Mandell, Arnold J.; Geyer, Mark A. Department of Psychiatry, University of California, San Diego, La Jolla, CA 92037 **Effects of amphetamines on regional tryptophan hydroxylase activity and synaptosomal conversion of tryptophan to 5-hydroxytryptamine in rat brain.** Journal of Pharmacology and Experimental Therapeutics. 189(3):676-689, 1974.

The effects of amphetamines on regional tryptophan hydroxylase activity and synaptosomal conversion of tryptophan to 5-hydroxytryptamine (5tHT) were examined in rat brain. The acute administration of d-amphetamine, methamphetamine, p-chloramphetamine, and l-amphetamine reduced the conversion of tryptophan to 5-HT in synaptosomes from the rat striatum. d-Amphetamine was approximately twice as potent as l-amphetamine in decreasing conversion activity. In contrast, fenfluramine increased this index of nerve ending 5-HT biosynthesis. The activity of solubilized tryptophan hydroxylase in the striatal synaptosomes was decreased by d-amphetamine treatment to the same extent that conversion activity was, accounting for the decrease in conversion activity. Tryptophan hydroxylase activity in the lateral midbrain after d-amphetamine was decreased to the same extent that it was in the nerve ending, but the decrease in the lateral midbrain preceded that observed in the nerve ending. The two major amphetamine metabolites in the rat, p-hydroxyamphetamine and p-hydroxynorephedrine, failed to influence regional tryptophan hydroxylase activity or synaptosomal conversion of tryptophan to 5-HT. The short latency of amphetamine induced changes in nerve ending 5-HT synthetic activity contrasts with the delay of days to weeks in response to such agents as lithium and morphine as have been previously reported. 36 references. (Author abstract modified)

186675 Guidotti, A.; Costa E. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **A role for nicotinic receptors in the regulation of the adenylate cyclase of adrenal medulla.** Journal of Pharmacology and Experimental Therapeutics. 189(3):665-675, 1974.

The activities of phosphodiesterase and adenylate cyclase and the concentration of catecholamines, 3',5'-cyclic adenosine monophosphate (cAMP) and protein in the capsule, cortex and medulla of normal and denervated adrenals were measured. Denervation reduces the concentrations of catecholamines and the activity of a denylate cyclase in medulla. All the other parameters are unchanged by denervation. Exposure to 4 C degrees causes the accumulation of cAMP in cortex and medulla; denervation reduces cAMP accumulation in medulla but not in cortex. Carbamylcholine increases the cAMP concentrations in adrenal cortex and medulla of intact and denervated adrenal. Bethanechol is less active than carbamylcholine in increasing cAMP concentrations of adrenal tissues. Mecamylamine and hexamethonium fail to change cAMP concentrations in adrenal parts but block the increase of cAMP elicited by either cold exposure or by carbamylcholine injections. Hexamethonium blocks the increase of cAMP elicited by cold exposure in cortex of denervated adrenal. Injections of epinephrine, tyramine, isoproterenol and amphetamine in doses that increase the concentrations of cAMP in other tissues fail to increase cAMP concentrations in adrenal medulla. Carbamylcholine increase the rate of cAMP accumulation in slices of adrenal medulla but fails to change that of cortical slices. In contrast, adrenocorticotropin stimulates cAMP accumulation in slices of adrenal cortex but not in slices of adrenal medulla. 28 references. (Author abstract modified)

186676 Westfall, Thomas C.; Brasted, Mary. Department of Pharmacology, University of Virginia School of Medicine, Charlottesville, VA 22903 **Specificity of blockade of the nicotine-induced release of 3H-norepinephrine from adrenergic neurons of the guinea-pig heart by various pharmacological agents.** Journal of Pharmacology and Experimental Therapeutics. 189(3):659-664, 1974.

A comparison was made of the ability of several pharmacological agents to alter the release of 3H-norepinephrine induced by nicotine with that of tyramine, potassium chloride and aminophylline. The following agents produced greater than 90% inhibition of nicotine induced release of 3H-norepinephrine: hexamethonium, morphine, cocaine, bretylium and lidocaine. Cocaine and bretylium decreased the release by tyramine, but only lidocaine decreased the release induced by potassium chloride. None of these agents decreased the release of 3H-norepinephrine by aminophylline. Colchicine produced a significant decrease in the release by nicotine but not tyramine or potassium chloride. Prostaglandins E1 and E2 decreased the release of 3H-norepinephrine by nicotine, potassium chloride and aminophylline but not tyramine. It is concluded that lidocaine blocks the nicotine induced release of norepinephrine by a local anesthetic action on the adrenergic axonal membrane to of the guinea pig heart whereas hexamethonium acts by blocking the nicotinic receptor. Colchicine appears to be producing a specific anticholinergic effect in decreasing the release of norepinephrine. 17 references. (Author abstract modified)

186677 Haeusler, G.; Lorez, H. P.; Bartholini, G.; Kettler, R.; Tranzer, J. P. F. Hoffmann-La Roche & Co., Basel, Switzerland **Absence of degeneration of adrenergic neurons after prolonged treatment with debrisoquin.** 189(3):646-658, 1974. Journal of Pharmacology and Experimental Therapeutics.

The absence of degeneration of adrenergic neurons after prolonged treatment with debrisoquin is reported in rats. Twenty four hours after termination of the 6 or 11 week treatment with debrisoquin, diminution of the effect of sympathetic nerve stimulation in isolated perfused renal arteries and the isolated vas deferens, a decrease in the norepinephrine content of various organs and a reduction of the intensity of formaldehyde induced catecholamine fluorescence of the long adrenergic neurons were observed. These alterations were completely reversible after discontinuation of the debrisoquin treatment. Pharmacological, biochemical, histological, histochemical and ultrastructural investigations did not reveal any signs of permanent functional impairment or of degeneration of the adrenergic neurons after prolonged treatment with debrisoquin. 36 references. (Author abstract modified)

186678 Choe, Jae-Yne; Peng, Tai-Chan. Department of Pharmacology, Northwestern University Medical School, Chicago, IL 60611 **Effect of 5-methoxytryptamine on serum calcium and phosphate in rats.** Journal of Pharmacology and Experimental Therapeutics. 189(3):593-602, 1974.

The effect of 5-methoxytryptamine (5-MT) on serum calcium and phosphate in rats was examined. Injection of 5-MT caused a rapid phatemia in rats. With pargyline it was possible to dissociate these two responses. Although concurrent administration of pargyline and 5-MT abolished the hypocalcemia found after 5-MT alone, it strikingly enhanced the 5-MT induced hyperphosphatemia. Thus the results indicate that production of hyperphosphatemia is not responsible for the fall in serum calcium induced by 5-MT. 5-MT produced hypocalcemia and hyperphosphatemia both in thyroidectomized and parathyroidectomized rats, indicating that these effects were not mediated either by the thyroid or by the parathyroid glands. Results of structure activity suggest that the methylation of serotonin at position 5 of the indole nucleus and the presence of a free amino group at position three (as represented by 5-MT) are required for the hypocalcemic effect; the amino group may need to be metabolized further since pargyline abolished the hypocalcemic action. The free

amino group at position three and the concomitant presence of either a hydroxyl or a methoxyl group at position five as found in serotonin and 5-MT respectively, appear to be essential for the production of hyperphosphatemia. 15 references. (Author abstract modified)

186681 Adkins, Elizabeth K.; Mason, Paul. Department of Psychology, Bucknell University, Lewisburg, PA 17837 **Effects of cyproterone acetate in the male Japanese quail.** Hormones & Behavior. 5(1):1-6, 1974.

The effects of cyproterone acetate in the male Japanese quail were studied. Ss were injected with oil or with one of four dosages of cyproterone acetate for 8 days. Copulatory behavior and cloacal gland size were measure daily. Cyproterone acetate reduced cloacal gland size at all dosages and in two experiments reduced copulation in eight out of 17 males at the two highest dosages. It is concluded that cyproterone acetate results in reproductive changes in at least two classes of vertebrates, and has behavioral as well as morphological effects. 19 references. (Author abstract)

186693 Cohen, Marlene L.; Trevor, Anthony J. Roche Institute of Molecular Biology, Nutley, NJ 07110 **On the cerebral accumulation of ketamine and the relationship between metabolism of the drug and its pharmacological effects.** Journal of Pharmacology and Experimental Therapeutics. 189(2):351-358, 1974.

The cerebral accumulation of ketamine and the relationship between metabolism of the drug and its pharmacological effects were examined. Rat brain slices accumulated ketamine rapidly to levels 23 times higher than those in the incubation medium. The process was saturable but was not influenced by 2,4-dinitrophenol or sodium iodoacetate. Equilibrium dialysis studies demonstrated no selective binding of ketamine to subcellular components of rat brain homogenates. Determination of the partition coefficients of ketamine and its N-demethylated product (metabolite I) indicated that both compounds were highly lipid soluble which may account for their rapid accumulation by cerebral tissues. The i.v. administration of metabolite I to rats caused central nervous system effects including hypnosis, ataxia and agitation, but of shorter duration than equivalent doses of ketamine. Brain levels of metabolite I required to maintain hypnotic effects were determined to be 33 micrograms per gram of tissue. The pretreatment of rats with phenobarbital caused a five fold increase in the rate of ketamine metabolism by hepatic tissue in vitro, whereas SKF 525-A pretreatment inhibited ketamine metabolism by 35% and prolonged the half-life of the drug in vivo. Neither pretreatment had significant effects on the duration of hypnosis caused by ketamine, but phenobarbital pretreatment decreased and SKF 525-A pretreatment increased, the duration of posthypnotic ataxia and agitation. 23 references. (Author abstract modified)

186694 Uretsky, Norman J. Neurology Research Laboratory, 300 Longwood Ave., Children's Hospital Medical Center, Boston, MA 02115 **Effect of alpha-methyldopa on the metabolism of dopamine in the striatum of the rat.** Journal of Pharmacology and Experimental Therapeutics. 189(2):359-369, 1974.

The mode of action of alpha-methyldopa in depleting dopamine (DA) levels in the rat striatum was studied. After the administration of alpha-methyldopa, the maximum accumulation of alpha-methyldopamine (MDA) occurred at 4 hours, the time of the maximal reduction in DA concentration. 6-Hydroxydopamine pretreatment markedly reduced the accumulation of MDA suggesting that this accumulation mainly occurs in DA containing neurons. After alpha-methyldopa administration, the concentrations of DA and its metabolites dihydroxyphenylacetic acid and homovanillic acid declined between 1 and 4 hours and then began to recover. Pargyline, administered 1 hour after alpha-methyldopa, prevented the further decline in DA suggesting that the decrease in DA required the deamination of DA by monoamine oxidase. Alpha-methyldopa pretreatment also decreased the amount of DA that accumulated 10 minutes after pargyline. The inhibitory effect of pargyline on monoamine oxidase activity was the same in both the alpha-methyldopa treated and control groups. Alpha-methyldopa treatment reduced the accumulation of 3H-DA and 3H-metabolites in the striatum 10 minutes after the intraventricular injection of 3H-tyrosine. These observations suggest that the decrease in the striatal DA concentration after alpha-methyldopa administration is mainly due to a decrease in the rate of DA synthesis. 43 references. (Author abstract modified)

186695 Lydiard, R. B.; Sparber, S. B. Department of Pharmacology, University of Minnesota, 105 Millard Hall, Minneapolis, MN 55455 **Evidence for a critical period for postnatal elevation of brain tyrosine hydroxylase activity resulting from reserpine administration during embryonic development.** Journal of Pharmacology and Experimental Therapeutics. 189(2):370-379, 1974.

Evidence for a critical period for postnatal elevation of brain tyrosine hydroxylase(TH) activity resulting from reserpine administration during embryonic development is reported. At 10 days of development, brain TH activity in reserpine treated embryos was not significantly different from vehicle injected or uninjected controls, although catecholamines were significantly reduced. By 15 days of embryonic development, TH activity increased four fold and reserpine treatment caused a significant increase in enzyme activity over controls. By 20 days of development TH activity increased an additional 8.5fold, to about 33 times the activity at 10 days, but between this time and 29 days of age after hatching TH activity increased only an additional 40%. Most important, however, is the continued significantly elevated TH activity at 29 days of age in the reserpine treated group, suggesting a longer lasting effect upon enzyme activity than has been shown previously. The data support the contention that nervous activity is essential for compensatory induction or activation and that a critical period for a set point of enzymatic activity may exist during development. 33 references. (Author abstract modified)

186698 Gintzler, Alan R.; Musacchio, Jose M. Department of Pharmacology, New York University Medical Center, New York, NY **Interaction between serotonin and morphine in the guinea-pig ileum.** Journal of Pharmacology and Experimental Therapeutics. 189(2):484-492, 1974.

In light of the inhibitory effects of 5-hydroxytryptamine (5-HT) on the ileum and its interactions with morphine in other tissues, the effect of 5-HT on the inhibitory response of the ileum to morphine was studied. Concentrations of 5-HT ranging from .02 micromolar to .2micromolar can potentiate the inhibitory effects of morphine, and vice versa; small concentrations of morphine (0.1micromolar) can potentiate the inhibitory response to 5-HT. Both of these effects can be abolished by washing. This potentiation is also observed with both nalorphine and methadone and seems to be due to a specific interaction between 5-HT and narcotic analgesics. Similar concentrations of 5-HT have no effect on the inhibition produced by norepinephrine, and norepinephrine itself has no effect on

the inhibition produced by morphine. Lysergic acid diethylamide can antagonize the inhibitory effects of 5-HT but can also produce a marked potentiation of the response to morphine. The results suggest that 5-HT may play an essential role in the mechanism by which morphine induces analgesia in the central nervous system. 30 references. (Author abstract)

186699 Hollister, Alan S.; Breese, George R., Cooper, Barrett R. Biological Sciences Research Center, University of North Carolina School of Medicine, Chapel Hill, NC 27514 **Comparison of tyrosine hydroxylase and dopamine-beta-hydroxylase inhibition with the effects of various 6-hydroxydopamine treatments on d-amphetamine induced motor activity.** Psychopharmacologia (Berlin). 36(1):1-16, 1974.

The significance of central noradrenergic and dopaminergic neural systems for the locomotor stimulant effects of d-amphetamine were investigated in rats with depletions of norepinephrine, dopamine, or both catecholamines produced by treatment with either reserpine, L-alpha-methyl-tyrosine (MPT), 6-hydroxydopamine (6-OHDA), or the dopamine-beta-hydroxylase inhibitor 1-phenyl-2-(2-thiazolyl)-2-thiourea (U-14,624). In animals pretreated with reserpine, amphetamine stimulated locomotor activity was blocked by MPT but not by U-14,624 when amphetamine was given 1 h after these catecholamine synthesis inhibitors. In rats with chronic depletions of brain norepinephrine, dopamine, or both catecholamines produced by different 6-OHDA treatments, both amphetamine stimulated motor activity and stereotyped behavior were antagonized by treatments reducing dopamine or both catecholamines but not in animals in which brain norepinephrine was reduced. Results are consistent with the view that the locomotor stimulation and stereotyped behaviors produced by d-amphetamine are dependent upon functional dopaminergic neural systems in brain. 57 references. (Author abstract)

186701 Meliska, Charles J.; Sawicky, Thomas E. Psychology Department, Monmouth College, Monmouth, IL 61462 **Differential effects of pilocarpine and scopolamine on the performance of a light-dark discrimination maintained by electrical stimulation of the brain.** Psychopharmacologia (Berlin). 36(1):29-39, 1974.

The differential effects of pilocarpine and scopolamine on the performance of a light - dark discrimination maintained by electrical stimulation of the brain (ESB) were studied. Four rats were first trained to make a light - dark discrimination by making ESB available to them for responses made in the presence of one stimulus (SD), but not in the presence of another stimulus (Sdelta). Subjects were then tested following treatment with pilocarpine, scopolamine, and combinations of the two. Pilocarpine significantly reduced the rate of reinforced responding, in the presence of SD but did not affect the rate of unreinforced responding, in the presence of Sdelta. On the other hand, scopolamine did not affect response rates during SD, but did significantly enhance responding during Sdelta. Furthermore, when given in combination, the two drugs failed to antagonize each other's actions. Instead, the outcome was equivalent to the sum of the two separate effects: i.e.,decreased responding during SD and increased responding during Sdelta. These results support the conclusions that a pilocarpine sensitive, inhibitory neural subsystem opposes response activation produced by ESB, in the presence of a discriminative stimulus (SD), and a separate muscarinic inhibitory system which is not sensitive to pilocarpine opposes the activation of nonreinforced responses, i.e.,in the presence of Sdelta. 25 references. (Author abstract)

186706 Cohen, Irving; Fischer, John F.; Vogel, Wolfgang H. Department of Pharmacology, Thomas Jefferson University, Philadelphia, PA **Physiological disposition of beta-phenylethylamine, 2,4,5-trimethoxyphenylethylamine, 2,3,4,5,6-pentamethoxyphenylethylamine and beta-hydroxymescaline in rat brain, liver and plasma.** Psychopharmacologia (Berlin). 36(1):77-84, 1974.

The fates of hydroxymescaline (HM), beta-phenylethylamine (PEA), 2,3,4,5,6-pentamethoxyphenylethylamine (PMPEA), a behaviorally active mescaline derivative, and of 2,4,5-trimethoxyphenylethylamine (TMPEA), a behaviorally inactive compound, were studied in rats. All compounds are quickly absorbed and distributed after i.p. injection and are also quickly removed from brain, liver and plasma. The compounds cross the blood - brain barrier differently and TMPEA could not be detected in the central nervous system explaining, perhaps, its lack of behavioral activity. A comparison of the minimal doses of these compounds which affect the CAR in rats is: PMPEA, mescaline, PEA, HM, in increasing doses, respectively. In contrast, a comparison of minimal brain levels necessary to affect the CAR reveals in increasing doses, the following relationship: PMPEA, mescaline, PEA. It is suggested that structure activity relationship studies with psychoactive compounds should not be based on injected doses but on actual brain levels at periods of abnormal behavior. 8 references. (Author abstract)

187075 Kadzielawa, K. Institute of Physiology, University of Aarhus, Universitetsparken, DK 8000 Aarhus C, Denmark **The action of alpha-methyldopa in the cerveau isole preparation.** Neuropharmacology (Oxford). 13(4):225-232, 1974.

The action of alpha-methyldopa in the cerveau isole preparation was examined. L-alpha-methyldopa infused i.v. elicits desynchronization in the electrocorticogram of the cerveau isole and rostropontine preparations, accompanied by mild mydriasis but not by changes in blood pressure. In gallamine immobilized cats with intact neuraxes only a tendency to desynchronization was noted. L-alpha-methyldopa induced desynchronization in the cerveau isole preparation was antagonized by previous injection of phenoxybenzamine and it was partly attenuated by propranolol. In reserpinized animals the action of L-alpha-methyldopa was more accentuated. The D-form of alpha-methyldopa has no significant action. It is suggested that desynchronization is mainly produced by L-alpha-methyldopamine formed from L-alpha-methyldopa in the brain. 46 references. (Author abstract)

187077 Sherman, A. D.; Mitchell, C. L. Department of Pharmacology, College of Medicine, University of Iowa, Iowa City, IA **Effect of morphine on regional levels of gamma-hydroxybutyrate in mouse brain.** Neuropharmacology (Oxford). 13(4):239-243, 1974.

Four experiments were performed on 340 male CFl mice to determine the effects of morphine and other agents on brain gamma-hydroxybutyrate (GHB) levels. Gas chromatographic analysis demonstrated that morphine produced a significant elevation of GHB levels. The increase occurred primarily in subcortical areas, and these effects were blocked by pretreatment with naloxon. Nonanalgesics failed to produce the same effect; the effect failed to occur in morphine tolerant animals. The dose response curve of the effect of morphine on GHB was nonlinear, and brain levels following morphine roughly follow the time course of analgesia. 2 references. (Author abstract)

187110 Walker, Judith Boas. Laboratory of Neurobiology, Ethel Percy Andrus Gerontology Center, University of Southern California, Los Angeles, CA **The effect of lithium on hormone-sensitive adenylate cyclase from various regions of the rat brain.** Biological Psychiatry. 8(2):245-251, 1974.

The effect of lithium ions on adenylate cyclase activity in homogenates from rat caudate, cerebellum, hippocampus, and brain stem, and from a crude subcellular fraction of cerebral cortex was examined. Lithium depressed the basal activity of the enzyme in each region, except in cerebellum and brain stem, and had no effect on the stimulation of the cyclase by dopamine. In contrast, the ion abolished the norepinephrine induced activation in cortex, hippocampus, but not in caudate, cerebellum, or brain stem. 25 references. (Author abstract)

187112 Mosnaim, A. David; Inwang, Edet E.; Sabelli, Hector C. Department of Pharmacology, Chicago Medical School, University of Health Sciences, Chicago, IL **The influence of psychotropic drugs on the levels of endogenous 2-phenylethylamine in rabbit brain.** Biological Psychiatry. 8(2):227-234, 1974.

The influence of psychotropic drugs on the level of endogenous 2-phenylethylamine (PEA) was studied in rabbits. PEA was found in the cerebral cortex, cerebellum and brain stem of the rabbit. The administration of L- or D-phenylalanine, delta9-tetrahydrocannabinol (acute), imipramine (acute or chronic), or pargyline (chronic) increased brain PEA levels. Chlorpromazine (acute or chronic), iprindole (acute or chronic), or isocarboxazid (chronic) did not significantly alter brain PEA levels. 29 references. (Author abstract)

187130 Nickander, Rodney; Booher, Richard; Miles, Henry. Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN 46206 **Alpha-l-acetylmethadol and its N-demthylated metabolites have potent opitate action in the guinea pig isolated ileum.** Life Sciences (Oxford). 14(10):2011-2017, 1974.

Alpha-l-acetylmethadol (LAM) and its N-demethylated metabolites were examined for opiate action in the guinea pig isolated ileum. Alpha LAM and its N-demethylated metabolites alpha-l-noracetylmethadol (NAM) and alpha-l-dinoracetylmethadol (NNAM) exhibited opiate like actions in vitro by depressing the electrically induced twitch of the longitudinal muscle of the guinea pig ileum. These effects were reversed by the opiate antagonist naloxone. The effect of both NAM and NNAM was approximately 15 times greater than LAM. The 50% inhibitory concentrations of the metabolites were well below those levels in plasma reported for man. The long duration of action of LAM as an opiate substitute is suggested to be due to the conversion to its metabolites. 18 references. (Author abstract)

04 MECHANISM OF ACTION: BEHAVIORAL

182211 Richardson, J. S.; Jacobowitz, D. M. Laboratory of Clinical Science, NIMH, Bethesda, MD 20014 **Behavioral effects of simultaneous depletion of brain norepinephrine and serotonin.** Federation Proceedings. 32(3):754, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the behavioral effects of simultaneous depletion of brain norepinephrine and serotonin were reported. Sixteen days after simultaneous stereotaxic injection of 6-hydroxydopa (6-HDP) and 5,6-dihydroxytryptamine (5,6-DHT) into the lateral ventricles of rats, there is a reduction of norepinephrine (NE) and serotonin (5-HT) in the telencephalon, diencephalon mesencephalon, cerebellum, and spinal cord. In the pons medulla, only NE is reduced. Brain dopamine is not affected. It was concluded that the increased emotionality of the 6-HDP treated rats might be due to the imbalance between the NE and the 5-HT levels in the brain; this supports the hypothesis that a relative increase in 5-HT activity over NE activity produces an increase in emotional arousal (anxiety). (Author abstract modified)

182215 Baxter, Bruce L.; Gluckman, Melvyn I.; Scerni, Rosemary. Wyeth Laboratories Inc., Box 8299, Philadelphia, PA 19101 **Differential self-injection behavior produced by fenfluramine versus other appetite inhibiting drugs.** Federation Proceedings. 32(3):754, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the differential self-injection behavior produced by fenfluramine versus other appetite inhibiting drugs was reported. Female rats had a Weeks type cannula permanently implanted into a jugular vein. Chlorphentermine, phenmetrazine, diethylpropion, d-amphetamine and Wy-13,828 (5-(p-chlorophenyl)-2,3-dihydro-5H-imidazo(2,1-a)isoindole, hydrochloride) all produced self-injection behavior in contrast to fenfluramine, which never produced such behavior in naive animals nor sustained self-injection behavior in animals first trained to self-inject cocaine. The effect of these compounds on spontaneous motor activity of rats was examined. All except fenfluramine and chlorphentermine showed stimulant activity. These data indicate that there is no simple correlation between the stimulant properties of an appetite inhibitor and its ability to reinforce self-injection. (Author abstract modified)

182217 Spaulding, Theodore C.; Dewey, William L. Department of Pharmacology, University of North Carolina, Chapel Hill, NC 27514 **Interaction of the behaviorally active drug, phenitrone, a purported hashish and LSD antagonist, with several central neurochemical systems.** Federation Proceedings. 32(3):755, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the interaction of the behaviorally active drug, phenitron (I), a purported hashish and LSD antagonist, with several central neurochemical systems was reported. Acetylcholine (Ach) response in the isolated frog rectus abdominus was potentiated by small dose of I. The in vitro hydrolysis of acetylthiocholine and butylthiocholine by rat whole brain homogenate was inhibited by I. Mouse whole brain levels of serotonin were lowered and serotonin turnover rate was decreased by I. The data suggest that I, like many other centrally acting agonists and antagonists, affect more than one neurochemical system in the brain. (Author abstract modified)

182237 Barker, L. A. Department of Pharmacology, Mt. Sinai School of Medicine, City University of New York, New York, NY 10029 **Drugs, behavior and choline acetyltransferase.** Federation Proceedings. 32(3):785, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the relationship between drugs, behavior and choline acetyltransferase were reported. Changes in brain ChAc activity following drug treatment or operant conditioning were reported. Reserpine administered for 3 days in mice gave decrease in hippocampal ChAc but not in forebrain ChAc. Mice treated with inhibitors of ChAc, Naphthylvinyl pyridine methiodide (NVP) or its hydroxyethyl analog (NVPH) 3-5 hours prior to training were evaluated in a passive-avoidance paradigm. This treatment mimicked scopolamine and hippocampal lesions. Water deprived rats

conditioned to bar press for water in either spaced (2 weeks) or massed (3 days) training schedules, showed no change in hippocampal ChAc. It is concluded that ChAc activity per se is not a suitable index for the activity of hippocampal cholinergic synapses in the paradigms used. A better index would be the turnover of acetylcholine. (Author abstract modified)

182238 Berntson, Gary G.; Leibowitz, Sarah F.; Pohorecky, Larissa A. Rockefeller University, New York, NY 10021 **Central cholinergic (muscarinic) link in the attack-reflexive biting mechanism of cats.** Federation Proceedings. 32(3):785, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the central cholinergic (muscarinic) link in the attack reflexive biting mechanism of cats was reported. Intraperitoneal injections of muscarinic agonists in cats can induce biting attack on a rat and associated reflexive biting in response to tactile stimulation of the lip line. This attack could be blocked by peripheral pretreatment with atropine sulfate. Further investigation revealed that reflexive biting can also be induced by central injections of carbachol, a cholinergic agonist with both muscarinic and nicotinic actions. Unilateral midbrain or hypothalamic injections of carbachol produced reflexive biting which was elicitable exclusively, or more readily, by touching the side of the lip contralateral to the injection site. The findings suggest that there is a central muscarinic link in the attack reflexive biting mechanism of cats. (Author abstract modified)

182239 Groblewski, G. E.; Coan, Mary; Zirzow, G. Woodard Research Corporation, Herndon, VA 22070 **Inhibition of isolation-induced aggression in the mouse by anticholinergic compounds.** Federation Proceedings. 32(3):785, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the structure activity relationship for the ability to inhibit isolation induced aggression in the mouse was determined for a series of anticholinergic compounds. Comparison of intravenous ED50's showed that the decreasing order of activity is scopolamine-atrocine greater than 1-hyoscyamine-atropine-apoatropine greater than homatropine-eucatropine. Tetrahydroaminacrine administered prophylactically, temporarily antagonized the stimulatory effect of scopolamine on mouse locomotor activity but failed to alter the regression curve for scopolamine induced inhibition. The results indicate that the isolation induced aggressive mouse may not be a useful model in which to test for antagonists to anticholinergic hallucinogens. (Author abstract modified)

182240 Malick, J. B.; Barnett, A. Department of Pharmacology, Schering Corporation, Bloomfield, NJ 07003 **Inhibition of isolation-induced aggression in mice by antiserotonergic drugs.** Federation Proceedings. 32(3):785, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the inhibition of isolation induced aggression in mice by antiserotonergic drugs was reported. The serotonin receptor antagonists methysergide (M), cinanserin (Ci), pizotyline (P), xylamidine (X), and cyproheptadine (Cy) were found to inhibit isolation induced aggression (IIA) in male mice. Antagonism of 5HTP induced head twitch was used as an in vivo measure of antiserotonin (A-S) activity, and physostigmine induced lethality was an in vivo measure of anticholingergic (A-C) activity in mice. All of the serotonin receptor antagonists tested inhibited IIA in doses similar to those antagonizing 5HTP. M and Ci are serotonin antagonists with little or no A-C activity, whereas P, X and Cy possessed significant A-C activity in addition to their A-S activity. The results suggest a possible relationship between serotonergic activity in the CNS and isolation induced fighting behavior in male mice. (Author abstract modified)

182241 Bernard, Bruce K.; Paolino, Ronald M. Section of Pharmacology and Toxicology, University of Connecticut, Storrs, CT 06268 **The use of biochemical correlates for the prediction of muricidal behavior in the wild rat.** Federation Proceedings. 32(3):785, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the use of biochemical correlates for the prediction of muricidal behavior in the wild rat was discussed. Muricidal behavior was determined in twenty wild Norwegian rats (Rattus norvegicus). Killers were defined as animals killing within 1 minute while nonkillers did not kill over the entire 12 hour session. Subsequent to testing, the brains were removed and the steady state levels of norepinephrine, dopamine, serotonin and 5-hydroxyindoleacetic acid in the cortex, hypothalamus, limbic system and medulla - pons were measured. Killing behavior was found to be best correlated with an increase in medulla - pons norepinephrine and a decrease in hypothalamic serotonin. Neither isolation nor learning had a significant effect upon this muricidal behavior. (Author abstract modified)

182242 Miller, F. P.; Gauger, D.; Garske, G. Lakeside Lab, Milwaukee, WI 53201 **Behavioral effects of EX 11-582A, a potential anti-psychotic agent.** Federation Proceedings. 32(3):785, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the behavioral effects of EX 11-582A (2-chloro-11-(3-dimethyl amino-propylidine) morphanthridine) studied in mice, rats, cats, and squirrel monkeys were reported. Preliminary screening in mice showed the compound to possess marked CNS depressant activity along with slight anticholinergic activity. Spontaneous motor activity in mice (photocell activity cages) was depressed by 50%. In cats, EX 11-582A exhibited depressant activity in doses as low as 0.125mg/kg. Similar effects were observed in squirrel monkeys, but the minimum effective dose was found to be about 1mg/kg. The results suggest that EX 11-582A has potential antipsychotic activity of a somewhat different nature from currently existing antipsychotic agents. (Author abstract modified)

182253 Tseng, L. F.; Hitzemann, R. J.; Loh, H. H.; Sutherland, V. C. Langley Porter Neuropsychiatric Institute, San Francisco, CA 94122 **Comparative effects of dl-p-methoxyamphetamine and d-amphetamine on central catecholamines and locomotor activity.** Federation Proceedings. 32(3):815, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, a comparison of the effects of dl-p-methoxyamphetamine (PMA) and d-amphetamine (A) on release and reuptake of 3H-NE and 3H-DA in tissue slices prepared from discrete areas of the rat brain was reported. PMA was found to be equipotent to or more potent than A in increasing release of 3H-NE from nonstriatal regions but was much less effective than A in increasing the release of 3H-NE or 3H-DA from the neostriatum. PMA was slightly more effective than A in blocking reuptake of 3H-NE into brain stem but was less potent than A in blocking the uptake of 3H-DA and 3H-NE in cortex and neostriatum. PMA did not increase the locomotor activity at a dosage (range 3-10mg/kg) at which A is effective. The results indicate that activation of both central NE and DA receptors are important for locomo-

tor activity and explain the difference in psychomotor stimulation by low doses of PMA and A. (Author abstract modified)

182258 Ts'o, Timothy O. T.; Chenoweth, Maynard B. Dow Chemical Company, Midland, MI 48640 **Similarity of chronic chlordiazepoxide treatment and removal of conflict situation.** Federation Proceedings. 32(3):817, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the similarity of chronic chlordiazepoxide (CDP) treatment and removal of conflict situation was examined. Five Sprague-Dawley adult male rats were food deprived and trained daily to obtain about 40% of their daily food ration under a described schedule. Daily CDP treatment 20 minutes before behavioral testing for three weeks increased the rate of responding of all animals. Disinhibition effects of CDP disappeared abruptly upon treatment cessation. The same animals continued on test daily. Foot shock was removed for two weeks and then was reintroduced. The changes in the animal behavior under shock - off and shock - on states were similar to CDP - on and CDP - off, respectively. It is suggested that the disinhibition effect of CDP which nullifies the noxious effect of foot shock in animals is comparable to the psychopharmacological effect on other noxae in man. (Author abstract modified)

182553 Yamazaki, Yutaka. Department of Anesthesiology, Tokyo Women's Medical College, Tokyo, Japan **Effects of phenothiazines, antihistamines, benzodiazepines and butyrophenones on the rhythms of wakefulness-sleep cycle in rats.** Journal of Tokyo Women's Medical College (Tokyo). 43(1/2):78-87, 1973.

The effects of various tranquilizing and sedative agents on the wakefulness - sleep cycle were studied in rats with chronically implanted brain electrodes. In spite of tranquilizing and sedative effects in man, each group of agents modified the wakefulness - sleep cycle in different manners. In animals, chlorpromazine and triflupromazine decreased wakefulness and increased slow wave sleep. Nitrazepam and haloperidol increased wakefulness and decreased slow wave sleep. Promethazine, hydroxyzine and diazepam induced bi-phasic changes: decrease of wakefulness with small doses and its increase with higher doses. All agents studied induced dose related decreases of the paradoxical phase of sleep. 32 references. (Author abstract modified)

182554 Yamazaki, Yutaka. Department of Anesthesiology, Tokyo Women's Medical College, Tokyo, Japan **Effects of phenothiazines, antihistamines, benzodiazepines and butyrophenones on electroencephalogram and feeding behavior of rats.** Journal of Tokyo Women's Medical College (Tokyo). 43(1/2):88-94, 1973.

The effect of various tranquilizing and sedative agents on feeding behavior was studied in rats with chronically implanted brain electrodes. Feeding quantity was increased remarkably with higher doses of promethazine, diazepam and nitrazepam, and slightly with chlorpromazine. It was decreased with triflupromazine and haloperidol. No change in feeding was induced with hydroxyzine. It was confirmed that diazepam induced stimulation of appetite with resultant weight gain by an experiment in mice. It was found that diazepam had two quite dissimilar effects, i.e.,the sedative effects were manifested by a decrease of wakefulness in behavior and electroencephalogram and the stimulant effect on appetite. 10 references. (Author abstract modified)

182762 Berry, P. A.; Lister, R. E.; Beattie, I. A. Inveresk Research International, Musselburgh, Midlothian, Scotland **Oxypertine and primate behaviour.** Postgraduate Medical Journal (Oxford). 48(Suppl. 4):11-14, 1972.

The effects of anxiolytic drugs on the behavior of five baboons was discussed in a symposium on the pharmacology and clinical use of oxypertine in anxiety held at Cambridge in 1972. The drugs tested were chlordiazepoxide, diazepam, medazepam and oxypertine. The animals were observed by closed circuit television and by an investigator who entered the cage to stimulate aggressive behavior. The tests suggest that the suppression of aggression in primates by drugs may be a useful test for drugs believed to possess anxiolytic or antipsychotic activity. The method of obtaining results used in this study is quick and requires few animals. In the case of human intrusion experiments, the dose levels required are similar or equal to those required for humans. The use of a species which is more closely related to man both socially and often metabolically is more meaningful and it is therefore suggested that baboons supplant the more commonly used mouse and rat for such testing purposes. 11 references. (Author abstract modified)

182859 Holtzman, Stephen G. Dept. of Pharmacology, Emory Univ., Atlanta, GA 30322 **Behavioral effects of morphine and opioid antagonists.** Final Report, NIMH Grant MH-19708, 1972, 4 p.

The role of cholinergic mediation in the behavioral effects of morphine was investigated, and the stimulant effects of narcotic antagonists on behavior were studied in the rat. In addition the specificity of the agonistic effects of pentazocine and cyclazocine was assessed. In experiment one, morphine produced an increase in the rate of avoidance responding. Scopolamine and methscopolamine produced no effects on operant behavior when administered alone but both significantly potentiated the increase in responding produced by morphine. Findings fail to support the concept that some of morphine's behavioral actions are mediated by central cholinergic systems. In experiment two, pentazocine and cyclazocine both increased avoidance responding and locomotor activity in a graded manner over a broad range of doses, and also produced dose related decreases in brain catecholamine content. In experiment three, naloxone blocked the effects of the narcotic antagonist analgesics on operant behavior, but not their effects on locomotor activity and brain catecholamine levels. It is concluded that narcotic antagonist analgesics may act as stimulants of behavior in the rat and that the agonistic component may be mediated by two distinct mechanisms: one blocked by naloxone and one which is not. These experiments have demonstrated dose related effects of narcotic antagonist analgesics that are not antagonized by naloxone.

183206 Burov, Yu. V.; Speranskaya, N. P. Institute of Pharmacology of the USSR Academy of Medical Sciences, Moscow /**The effect of psychotropic agents on the formation of avoidance reaction in albino rats during electropain stimulation of another rat.**/ Vliyaniye psikhotropnykh veshchestv na obrazovaniye reaktsii izbeganiya u belykh krys pri elektrobolevom razdrazhenii drugoy osobi. Byulleten' Eksperimental'noy Biologii i Meditsiny (Moskva). 76(10):59-61, 1973.

The effect of psychotropic agents on the formation of avoidance reaction in albino rats during electropain stimulation of another rat was studied. Amphetamine, imipramine, haloperidol and droperidol were administered daily to rats for a period of 10 days; their effect on the formulation of

avoidance reaction in albino rats in response to pain reaction of another rat is noted. It was found that all the mentioned agents stimulate the formation of avoidance reaction. In some rats this reaction is retained after the administration of the psychotropic agents is suspended. The most active is imipramine. The stimulating effect is apparently associated with the adrenopositive properties of the agents under study. 13 references. (Journal abstract modified)

183470 Ziskind, D.; Baum, M.; Amit, Z. Center for Research on Drug Dependence, Sir George Williams University, Montreal, P.Q., Canada **Failure of ACTH to influence avoidance extinction in a one-way avoidance situation.** Bulletin of the Psychonomic Society. 2(6B):425-426, 1973.

The failure of ACTH to influence avoidance extinction in a one way avoidance situation is reported. Forty rats were trained to avoid shock in a one way automated ledge box. After acquisition of the avoidance response, the rats were administered an injection of Ringer's solution or one of three dosages of ACTH dissolved in Ringer's solution. Ten minutes after injection, the animal was replaced in the avoidance apparatus with the shock disconnected, and the number of trials required to extinguish the avoidance response was determined. The hypothesis that the increase in resistance to extinction of shock avoidance observed after ethanol injections is related to increased cirulating ACTH levels was tested. The results did not support the hypothesis. 10 references. (Author abstract modified)

183517 Selivanova, A. T.; Egorova, N. L. I.P. Pavlov Physiological Division, Institute of Experimental Medicine, Leningrad **/Changes in short-term and long-term memory of dogs and cats under the effects of amizyl (benactyzine)./** Izmeneniya kratkosrochnoy i dolgosrochnoy pamyati u sobak i koshek pri vozdeystvii amizilom. Farmakologiya i Toksikologiya (Moskva). 36(4):389-392, 1973.

Changes in short-term and long-term memory in cats and dogs under the effect of amizyl (benactyzine) were studied. Doses of 0.1to 0.2mg/kg of amizyl in dogs disturbed the short memory span. The closing of positive temporary connections was effected two to five times slower in cats that had been administered amizyl than in those of the control group; no inhibitory conditioned connections were realized at this juncture. Long-term memory was affected only after prolonged administration of amizyl lasting up to 20 days. At this time positive connections remained intact; the inhibitory connections redeveloped after withdrawal of the preparation. 13 references. (Journal abstract modified)

183606 Ahtee, Liisa. Department of Pharmacology, University of Helsinki, Siltavuorenpenger 10, SF-00170 Helsinki 17, Finland **Catalepsy and stereotyped behaviour in rats treated chronically with methadone: relation to brain homovanillic acid content.** Journal of Pharmacy and Pharmacology (London). 25(8):649-651, 1973.

In a letter to the editor, the behavior and brain homovanillic acid (HVA) content of rats treated chronically with methadone is reported. Results indicate that in rats treated chronically with methadone, tolerance develops towards the cataleptic effects of methadone but simultaneously the rats start gnawing and having other stereotypes. The duration of abnormal behavior (catlepsy and stereotypes) induced by a single dose of methodone was about the same as that of catalepsy in control rats. Methadone also increased the striatal HVA up to a similar amount in control and tolerant rats. It is suggested that the primary effect of methadone could be catalepsy which causes a compensatory increase in the production of dopamine. The additional dopamine then causes stereotyped behavior because the methadone induced catalepsy in tolerant rats lasts for only a short time. 8 references.

183790 Corcoran, M. E.; Amit, Z.; Malsbury, C. W.; Daykin, S. Kinsmen Laboratories Faculty of Medicine, University of British Columbia, Vancouver 8, Canada **Reduction in copulatory behavior of male rats following hashish injections.** Research Communications in Chemical Pathology and Pharmacology. 7(4):779-782, 1974.

The effects of cannabis administration on the copulatory behavior of sexually experienced male Hooded rats were examined. Both hashish doses (30 and 15 mg/kg) clearly depressed copulatory activity. The difference in number of animals copulating between the experimental and control groups was significant only under the drug conditions, where fewer animals receiving hashish injections copulated as compared to control subjects. There were no significant changes in copulatory activity within the control group due to injection of the vehicle, while the hashish group showed a significant treatment effect. Data suggests that the first hashish treatment may have had a residual effect, which would have contributed to the depression produced by the second, lower dose. In order to determine if the lower dose of hashish has an effect on copulation without pretreatment with the higher dose, three more vigorous copulators were tested under the low dose conditions. On the five injection days, these animals achieved only half as many successful copulations as they had on the five preceding baseline days, demonstrating that the low dose of hashish does disrupt copulation. 5 references.

183862 Millenson, J. R.; Leslie, J. Department of Psychology, McGill University, Montreal, Canada **The conditioned emotional response (CER) as a baseline for the study of anti-anxiety drugs.** Neuropharmacology (Oxford). 13(1):1-9, 1974.

The effects of major and minor tranquilizers on an animal analog of anxiety, the conditioned emotional response (CER), are surveyed. The apparent inconsistencies in results can be traced to drug interactions with acute versus chronic regimens of administration, and to the occasional failure to employ sensitive, stable behavioral baselines. The CER is analyzed into its relevant behavioral components, and an interactive motivational model is used to rationalize the effects of drug treatments. Although the evidence still remains far too fragmentary to evaluate the validity of the CER as a prototype of anxiety, human or animal, the technique is likely to continue to find a useful role as one element in the behavioral profile of pharmacological agents. 57 references. (Author abstract)

183863 Apfelbach, R.; Delgado, J. M. R. Zoophysiologisches Institut, Universitat Tubingen, 74 Tubingen, Holderlinstrasse 12, W. Germany **Social hierarchy in monkeys (Macaca mulatta) modified by chlordiazepoxide hydrochloride.** Neuropharmacology (Oxford). 13(1):11-20, 1974.

The effects of intramuscular injection of chlordiazepoxide (Librium) on individual and social behavior was tested on a colony formed by four rhesus monkeys. Behavior was quantified during three periods of 15 min each: first control (C I), delivery of pellets to an elevated feeder (CP) and second control (C II). Administration of 5mg/kg to the dominant monkey produced a 50% reduction of spontaneous mobility which lasted for several hours. The number of attacks increased significantly during C I, was not modified during CP and diminished during C II. It is postulated that chlordiazepoxide produced a decrease of normal signs of dominance and in-

creased the challenge and replacement of the nondrugged animal against the authority of the leader of the group. Increasing the dose injected into the dominant animal to 10mg/kg produced a greater and more lasting reduction of spontaneous mobility, with some cumulative effects, a reduction of walking during C I and C II, an absence of mounting and grooming and an increase of lying. Attacks also increased during C I and CP, while disappearing during C II. Injection of 10mg/kg of chlordiazepoxide into the lowest ranking monkey, did not modify his hierarchical position, nor did it produce any signs of hostility. His behavior was, however, modified, decreasing spontaneous mobility and walking, abolishing grooming and increasing lying down. 35 references. (Author abstract modified)

183889 Byrd, Larry D. New England Regional Primate Research Center, Harvard Medical School, Southborough, MA 01772 **Modification of the effects of chlorpromazine on behavior in the chimpanzee.** Journal of Pharmacology and Experimental Therapeutics. 189(1):24-32, 1974.

Modification of the effects of chlorpromazine on key pressing behavior in the chimpanzee was examined in a multiple schedule comprising a 10 minute fixed-interval schedule and a 30 response fixed-ratio schedule of food delivery. Presentation of a brief (20 msec) auditory stimulus after each response during the fixed-interval and fixed-ratio schedules potentiated the enhancing effect of chlorpromazine on responding under the fixed-interval schedule. Presentation of the brief stimulus did not alter the effects of chlorpromazine on responding under the fixed-ratio schedule and on water intake, however. Results show that chlorpromazine can enhance schedule controlled responding in the chimpanzee. The enhancing effect of chlorpromazine was potentiated when each response produces a brief change in environmental stimuli and chlorpromazine only affects water intake at doses that also disrupt responding. 15 references. (Author abstract modified)

183890 Branch, Marc N. Department of Psychology, University of Florida, Gainesville, FL 32611 **Behavior as a stimulus: joint effects of d-amphetamine and pentobarbital.** Journal of Pharmacology and Experimental Therapeutics. 189(1):33-41, 1974.

In a study of the joint effects of d-amphetamine and pentobarbital, pigeons were trained on a procedure where the number of pecks required on a center key (fixed-ratio) signalled which of two side keys was correct. The effects of d-amphetamine, pentobarbital and combinations of the drugs on both rate of responding and accuracy were examined. Response rates on the center key were increased by appropriate doses of pentobarbital, but only decreased by d-amphetamine. When given in combination, the two drugs antagonized each other's effects. Response rates on the side keys were increased by either d-amphetamine or pentobarbital, and combinations of the two drugs acted synergistically to increase rates more than either drug alone. Both drugs reduced accuracy in a dose related fashion, and combinations of low doses of the drugs worked synergistically to decrease accuracy. The effects of amphetamine were little changed when the difficulty of the discrimination was increased. The nature of the joint effect of amphetamine and pentobarbital depended on both the current situation and on the aspect of behavior measured. 18 references. (Author abstract)

183892 Holtzman, Stephen G. Emory University, Department of Pharmacology, Atlanta, GA 30322 **Behavioral effects of separate and combined administration of naloxone and d-amphetamine.** Journal of Pharmacology and Experimental Therapeutics. 189(1):51-60, 1974.

Dose response curves for d-amphetamine were determined in the rat for three distinct types of behavior: continuous avoidance responding, locomotor activity and food intake. The effects of d-amphetamine were also evaluated on locomotor activity and food intake in the mouse. d-Amphetamine was tested alone and in combination with naloxone, a specific narcotic antagonist that is almost devoid of agonistic properties. Characteristic amphetamine effects were observed in both species. Avoidance responding and locomotor activity were increased by low doses of d-amphetamine and were disrupted by higher doses. A similar biphasic dose response curve was generated for food intake in the rat, but d-amphetamine produced only a suppression of food intake in the mouse. Inactive doses of naloxone significantly and consistently reduced the stimulant effects of d-amphetamine on avoidance responding and locomotor activity in the rat. Naloxone itself showed pronounced activity in suppressing food intake in the rat. The results show that a narcotic antagonist can markedly modify the behavioral effects of a nonopioid psychoactive drug. Some of the actions of naloxone were species dependent. 25 references. (Author abstract modified)

183893 Kosersky, D. S.; McMillan, D. E.; Harris, L. S. Department of Pharmacology, College of Pharmacy and Allied Health Professions, Northeastern University, Boston, MA 02115 **Delta9-tetrahydrocannabinol and 11-hydroxy-delta9-tetrahydrocannabinol: behavioral effects and tolerance development.** Journal of Pharmacology and Experimental Therapeutics. 189(1):61-65, 1974.

The effects of intravenous injections of delta9-tetrahydrocannabinol (THC) and its hydroxylated metabolite, 11-hydroxy-delta9-tetrahydrocannabinol (11-OH-THC) were studied in pigeons, whose rates of key pecking were maintained by a variable interval 3 minute schedule of food presentation. A dose of 0.03mg/kg of either THC or 11-OH-THC produced an almost immediate decrease in the rate of key peck responding, with the rate of responding returning to control levels within 30 to 45 minutes after injection. Doses of 0.1-0.3mg/kg of either THC or 11-OH-THC completely eliminated responding immediately after injection with a gradual recovery of responding beginning within 60 to 90 minutes or 195 to 240 minutes. The gradual recovery of responding took place over a 60 to 90 minute period for both doses of THC and 11-OH-THC. Tolerance developed to successive daily injections of 0.3mg/kg of either THC or 11-OH-THC over an 8-15 day period and a reciprocal cross-tolerance was demonstrated between THC and 11-OH-THC. On the basis of these effects on the schedule controlled behavior of pigeons, THC and 11-OH-THC are indistinguishable. 20 references. (Author abstract)

184200 Stern, P.; Catovic, Sabira; Stern, M. Institut za Farmakologiju, Medicinskog Fakulteta, 71000 Sarajevo, Yugoslavia **Mechanism of action of substance P.** Archives of Pharmacology (Berlin). 281(2):233-239, 1974.

The mechanism of action of synthetic substance P (SP) (the natural polypeptide can be isolated from brain tissue) was studied in mice. SP raised glycine levels both in the brain and in the spinal cord. The synthetic polypeptide, as well as the single amino acid, abolished motor hyperactivity induced by beta,beta'-iminodipropionitrile in mice. The amino acid was effective even at very low intrinsic glycine levels, a condition where the polypeptide fails to act. It is suggested that SP action against exaggerated motorics is based on its increasing of spinal glycine which, in turn, inhibits the motor neurons. 33 references. (Author abstract)

184212 Masur, Jandira; Benedito, Marco Antonio Campana. Departamento de Psicobiologia, Escola Paulista de Medicina, Rua Botucatu, 862, 04023 Sao Paulo, Brazil **Inversion by apomorphine of the tendency of female rats to be defeated by males when competing for food in a straight runway.** Behavioral Biology. 10(4):527-531, 1974.

To determine whether the administration of apomorphine to female rats would modify their tendency to be defeated in the straight runway, 14 female rats competed for food in a straight runway against 14 male rats through a fixed pair procedure. The females won only 24 and 30%, respectively, in two experimental sessions of five contests each. The other 15 females were given 1.0mg/kg of apomorphine 10 min before the beginning of the contest session, while their 15 male partners received saline. Under drug action females won 65% of the contests. Forty eight hours later, the same females, which now received control solution, won only 15%. 11 references. (Author abstract)

184238 Amit, Z.; Cohen, J. Department of Psychology, Center for Research on Drug Dependence, Sir George Williams University, Montreal, Canada **The effect of hypothalamic stimulation on oral ingestion of diazepam in rats.** Behavioral Biology. 10(2):223-229, 1974.

The effect of hypothalamic stimulation on oral ingestion of diazepam was examined in rats. Under conditions of free choice between water and diazepam solutions, Albino rats were reluctant to drink diazepam solutions in all but the lowest concentrations. Prolonged exposure to diazepam solutions did not result in increased intake. Electrical stimulation of the lateral hypothalamus which was shown to induce a permanent preference for ethanol in rats, and a schedule of periodic withdrawal shown to increase intake of ethanol in rats both failed to induce a similar preference or increased intake of diazepam solutions. The findings are discussed in terms of the postulated generality of the effect of both hypothalamic stimulation and periodic withdrawal. 10 references. (Author abstract)

184242 Schaefer, Gerald J.; Buchanan, Denton C.; Ray, Oakley S. Psychology Research Laboratories, Veterans Administration Hospital, Nashville, TN **Effects of neonatal strychnine administration on active avoidance in rats.** Behavioral Biology. 10(2):253-258, 1974.

The effects of neonatal strychnine administration on active avoidance in rats were studied. Rat pups received strychnine sulphate or saline injections, handling, or no manipulation on days 2-5 after birth. An active avoidance task at 45 days showed no difference between the strychnine, saline, or handled groups, but all manipulated groups made significantly more avoidance responses than the nonhandled group. The data suggest that the behavioral effect of a central nervous system stimulant administered to neonatal rats may be altered by the physical manipulation involved in the drug administration. 19 references. (Author abstract)

184371 Golub, Mari; Kornetsky, Conan. Behavioral Pharmacology Laboratory, Boston University School of Medicine, Boston, MA 02118 **Seizure susceptibility and avoidance conditioning in adult rats treated prenatally with chlorpromazine.** Developmental Psychobiology. 7(1):79-88, 1974.

Offspring of female rats treated early in gestation with chlorpromazine (CPZ) were tested at 30 days of age for seizure susceptibility and at 90 days of age for shock avoidance learning. Fostering procedures permitted separation of prenatal influences from postnatal rearing influences of drug treatment. Offspring of drug treated mothers had higher avoidance scores, higher intertrial activity levels, and greater seizure susceptibility than offspring of controls. Animals reared by previously treated mothers also had higher avoidance and greater seizure susceptibility. This postnatal effect depended on sex and was not accompanied by an overall increase in intertrial activity. Rearing by a previously drug treated mother was also found to modify the influence of neonatal stress on adult avoidance learning. 40 references. (Author abstract)

184380 Porter, Alan L. Dept. of Engineering, FL-10, University of Washington, Seattle, WA 98105 **Effects of nonhydrogen-bonding anesthetics on memory in the chick.** Behavioral Biology. 10(3):365-375, 1974.

The effects of five nonhydrogen bonding anesthetics (NHBA) upon memory processing were studied in the neonate chick using a one trial peck avoidance and a one trial appetitive learning paradigm. No effects were observed with helium, nitrogen, or carbon dioxide, nor with hypoxia. Xenon induced a marginal amnesic effect and nitrous oxide induced a marginal enhancement. An environmental shift required to administer pressurized NHBA treatment (pressure to 9.4atmospheres) after training reduced subsequent pecking responses at 3 hr and/or 24 hr testing. Results are discussed in light of reported findings and theoretical implications of the NHBA for memory research. 22 references. (Author abstract)

184834 Murphy, Lawrence R.; Brown, Thomas S. DePaul University, Chicago, IL 60614 **Hippocampal lesions and learned taste aversion.** Physiological Psychology. 2(1):60-64, 1974.

Rats with hippocampal lesions were compared with neocortical and sham operated controls on a taste aversion learning task using an 8% sucrose solution (CS) and 2% body weight IP injection of .15 M lithium chloride (UCS). Hippocampally ablated animals acquired the taste aversion as rapidly as controls after a single CS-UCS pairing. No differences were found among the groups in terms of either the magnitude or extinction of the aversion. The results do not support a general loss of response inhibition interpretation of hippocampal function. The results confirm and extend a number of previous findings indicating that the enhanced perseverative tendencies frequently observed in rats with hippocampal lesions are absent in consummatory type tasks. 25 references. (Author abstract).

184838 Winocur, Gordon; Bagchi, S. P. Trent University, Peterborough, Ontario, Canada **Effects of bufotenine and p-chlorophenylalanine on reactivity to footshock.** Physiological Psychology. 2(1):75-79, 1974.

In two experiments, groups of rats were injected with bufotenine, p-chlorophenylalanine (PCPA), bufotenine + PCPA (B + PCPA), or saline, and their reactions to footshock were recorded during tests of distractability and response thresholds. Bufotenine consistently decreased sensitivity to shock, while PCPA produced the opposite effect. Individual effects of bufotenine and PCPA were not apparent in the B + PCPA groups, which, in both experiments, behaved like saline control groups. The results support the hypothesis that bufotenine and PCPA affect reactivity to external stimuli in opposite ways. 15 references. (Author abstract modified).

184953 Silbergeld, Ellen K.; Goldberg, Alan M. School of Hygiene and Public Health, Johns Hopkins University, Baltimore,

MD 21205 **Lead-induced behavioral dysfunction: an animal model of hyperactivity.** Experimental Neurology. 42(1):146-157, 1974.

The relationship between lead ingestion and behavioral dysfunction was studied in neonatal mice. Sucking mice were exposed to lead acetate from birth indirectly through their mothers and then directly after weaning. For the first 60 days, no deaths of offspring occurred due to lead but their growth and development were significantly retarded. Activity of offspring was measured between 40 and 60 days of age, and treated mice were more than three times as active as age matched controls. Treated and control animals were given drugs used in treatment and diagnosis of minimal brain dysfunction hyperactivity in children: d-amphetamine and l-amphetamine, methylphenidate, phenobarbital, and chloral hydrate. Lead treated hyperactive mice responded paradoxically to all drugs except chloral hydrate; amphetamine and methylphenidate suppressed hyperactivity, while phenobarbital increased levels of motor activity. Chloral hydrate was an effective sedative. 42 references. (Author abstract modified)

184979 Langfeldt, Thore. Institute of Neurophysiology, University of Oslo, Oslo, Norway **Diazepam-induced play behavior in cats during prey killing.** Psychopharmacologia (Berlin). 36(2):181-184, 1974.

The effects of diazepam on prey killing behavior in cats were investigated. Cats exhibiting prey killing can be divided into two categories by the appearance of prey play behavior: immediate killers that never exhibited prey play behavior and delayed killers that always exhibited play behavior prior to the mortal neckbite. Low doses of diazepam given to immediate killers induced prey play behavior and higher dosages increased the play period. The significance of the play behavior and possible underlying mechanisms of the drug action are discussed. 6 references. (Author abstract modified)

184980 Oglesby, M. W.; Winter, J. C. Dept. of Pharmacology, University of Chicago, Chicago, IL 60637 **Strychnine sulfate and piracetam: lack of effect on learning in the rat.** Psychopharmacologia (Berlin). 36(2):163-173, 1974.

The effects of posttrial administration of piracetam and strychnine sulfate were examined using learning tasks. In terms of two parameters used to assess drug effects on the acquisition of the discrimination, neither strychnine nor piracetam facilitated learning. In the second experiment, drug treated animals did not differ significantly from controls in their acquisition of the avoidance response in any of the six experiments. In all, eight doses of strychnine were tested, ranging from 0.005 to 0.60mg/kg. Analysis of variance showed no significant differences between any of the treatment conditions, nor was there evidence of a graded dose effect relationship. The present results do not support the conclusion that strychnine or piracetam facilitate learning. 29 references. (Author abstract modified)

185033 Albright, J. Donald; Goldman, Leon. Lederle Laboratories, American Cyanamid Company, Pearl River, NY 10965 **Alkaloid studies. 9. Preparation of 18-acylyohimban-17-ones and their conversion to new heterocyclic yohimbans.** Journal of Medicinal Chemistry. 17(3):296-300, 1974.

Heterocyclic derivatives of yohimban with an isoxazole, pyrazole, or pyrimidine ring attached to the E ring have been prepared by reaction of 18-acylyohimban-17-ones with hydroxylamine, hydrazine, guanidine, 2-methyl-2-thiopseudourea, and benzamidine. In order to find potentially useful depressants of the central nervous system, the compounds were screened to determine their effect on rod walking ability and locomotor activity of mice. In contrast to yohimbano (17,18-c)pyrazole, the 5'methyl substituted pyrazole required high doses to impair rod walking ability and locomotor activity of mice. These derivatives were the only ones in the report which exhibited motor depression (MDD50) at doses of 100mg/kg or less and all were relatively inactive in impairing rod walking ability. 8 references.

185265 Overstreet, David H. School of Biological Sciences, Flinders University of South Australia, Bedford Park, South Australia 5042, Australia **Reduced behavioral effects of pilocarpine during chronic treatment with DFP.** Behavioral Biology. 11(1):49-58, 1974.

The relation between low brain cholinesterase (ChE) activity and the reduced behavioral effects of pilocarpine was examined. Chronic treatment with 0.2mg/kg diisopropylfluorophosphate (DFP) per day did not significantly alter the FR5 responding of male rats even though brain cholinesterase (ChE) activity was reduced to below 30% of normal in 9 days. The behavioral depressant effects of pilocarpine on this task were reduced in the DFP treated animals as early as 5 days of treatment, when brain ChE activity was shown to be approximately 40% of normal. Challenges with other cholinergic agents confirmed earlier findings, thus supporting the hypothesis that both muscarinic and nicotinic receptors alter their sensitivity to acetylcholine during chronic DFP treatment. 24 references. (Author abstract)

185463 Berg, David; Baenninger, Ronald. Temple University, Philadelphia, PA 19122 **Predation: separation of aggressive and hunger motivation by conditioned aversion.** Journal of Comparative and Physiological Psychology. 86(4):601-606, 1974.

A dissociation between mouse killing and feeding is demonstrated in rats by using the conditioned aversion paradigm to suppress both mouse killing and feeding on the mouse independently. Rats were given lithium chloride 15 minutes after ingesting mice or saccharin on either 1 day or 4 days. Intake of both substances dropped in the 1 day trial groups but not in the 4 day trial groups. In a second experiment rats that received lithium chloride after killing mice they were not permitted to eat showed no changes in mouse killing. Rats permitted to feed on mice they had killed continued to kill but ate less after a single lithium chloride trial. Feeding and killing appear to be separable by this technique. 8 references. (Author abstract modified).

185705 Herndon, James G., Jr. Emory University **Neural and chemical mechanisms of female sexual behavior in the rat. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-Films, No. 74-10284 HC$10.00 MF$4.00 92 p.

The effects of lesions of ascending monoaminergic fiber systems and d-amphetamine on the sexual behavior of female albino rats were observed. It is noted that the most severe impairments in receptivity in response to ovarian hormones is observed in rats bearing lesions of the dorsal and ventral norepinephrine bundles (DV) or lesions in the region of Ungerstedt's A-10 dopamine producing cells. It is found that administration of d-amphetamine reliably enhances receptivity in estrogen and progesterone treated rats bearing DV or A-10 lesions. An excitatory role for catecholamines in female sexual behavior is postulated, with norepinephrine as the critical catecholamine in receptive behavior. It is hypothesized that female sexual behavior is under the control of mutally an-

tagonistic noradrenergic and serotonergic systems. (Journal abstract modified)

185727 Smith, William Merdoc, Jr. Univ. of Mississippi **Nalorphine as an aversive agent. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-Films, No. 74-11444 HC$10.00 MF$4.00 66 p.

The behavioral effects of an opiate antagonist, nalorphine, on morphine dependent rats were studied in three tests commonly used to identify stimuli as aversive: signalled avoidance, punishment of lever pressing, and maze punishment. Test procedures are described. It was found that, in the signaled avoidance study, nalorphine infusion produced avoidance responding in rats, similar to that produced by other aversive stimuli. Findings from the punishment of lever pressing study indicate significant decreases in responding rate under conditions of nalorphine infusion. While findings fail to show a significant contingency effect, they parallel results of early studies of contingent and noncontingent suppression effects of strong electric shock. In the maze punishment study, the group receiving nalorphine infusions switched preferences, while the saline group did not. Data indicated that response contingent nalorphine infusions have a punishing effect on behavior in the maze. It is concluded that the behavioral effects of nalorphine parallel the effects of more commonly used aversive stimuli, such as electric shock. (Journal abstract modified)

185748 Barry, Herbert, III; Steenberg, Marie L.; Manian, Albert A.; Buckley, Joseph P. Dept. of Pharmacology, Univ. of Pittsburgh, Pittsburgh, PA 15261 **Effects of chlorpromazine and three metabolites on behavioral responses in rats.** Psychopharmacologia (Berlin). 34(4):351-360, 1974.

Effects of chlorpromazine (CPZ) and three metabolites (3,7-dihydroxy-CPZ; 7,8-dihydroxy-CPZ; 7-hydroxy-CPZ) on behavioral performance of rats were tested by three methods: 1) continuous nondiscriminative lever pressing shock avoidance response without a warning signal; 2) discriminative pole climbing shock avoidance and escape; 3) discriminative control of behavior by drug stated. Both types of avoidance were much more impaired by CPZ than by the metabolites. The metabolite producing the most consistent impairment was 7-hydroxy-CPZ and the least consistent was 7,8-dihydroxy-CPZ. In the test for discriminative control of behavior by drug states, the 7-hydroxy-CPZ was the only metabolite which evoked the CPZ stimulus characteristics whereas the 7,8-dihydroxy-CPZ produced a generalized depressant effect. 14 references. (Author abstract modified)

185752 Dykstra, Linda A.; Appel, James B. Dept. of Psychology, University of North Carolina, Chapel Hill, NC 27514 **Effects of LSD on auditory perception: a signal detection analysis.** Psychopharmacologia (Berlin). 34(4):289-307, 1974.

The effects of LSD on perceptual behavior of rats were analyzed with a signal detection procedure. One experiment investigated the effect of LSD on the detection of tones of different frequencies; the other investigated LSD's effect on temporal discrimination. No dose or dosage regimen of LSD significantly altered the rat's ability to make the temporal or the frequency discrimination. LSD did, however, alter the rat's preference for responding on one of the two levers. These changes were significant following doses of LSD greater than 0.04mg/kg, and three doses of LSD given in a regimen designed to produce behavioral tolerance. 27 references. (Author abstract modified)

185753 Ellison, Gaylord D.; Bresler, David E. Dept. of Psychology, University of California, Los Angeles, CA 90024 **Tests of emotional behavior in rats following depletion of norepinephrine, of serotonin, or of both.** Psychopharmacologia (Berlin). 34(4):275-288, 1974.

Groups of rats were depleted of norepinephrine (using 6-hydroxydopamine, 6-OHDA), of serotonin (using chronic para-chlorophenylalanine, PCPA), or of both and were tested on a variety of behavioral tasks. Rats treated with 6-OHDA and rats treated with PCPA showed different and often opposed behavioral syndromes. Animals which received both drugs generally showed the greatest behavioral disruptions. PCPA rats showed decreased locomotion in quiet novel environments but increased locomotion when stimulated. Rats receiving 6-OHDA showed an initially decreased rate of rearing in open field and decreased sucrose consumption when food deprived. Results are discussed in terms of the reserpine model of depression. 26 references. (Author abstract modified)

185927 Allen, C.; Allen, Blair S.; Rake, A. V. Biophysics Dept., Pennsylvania State Univ., University Park, PA 16802 **Pharmacological distinctions between 'active' and 'passive' avoidance memory formation as shown by manipulation of biogenic amine active compounds.** Psychopharmacologia (Berlin). 34(1):1-10, 1974.

Pharmacological distinctions between active and passive avoidance memory formation as shown by manipulation of biogenic amine active compounds was explored. Female mice were trained either in passive step - through avoidance or in an active one way escape avoidance task. The apparent memory for either task (measured 8 days later) was reduced by reserpine dosage immediately after training. 5-Hydroxytryptophan (5-HTP), given along with the reserpine, eliminated memory reduction for the passive training; Dopa, given along with the reserpine, did not eliminate memory deficit for the passive training. 5-HTP given along with reserpine did not eliminate the memory deficit for the active training; Dopa given along with the reserpine did eliminate memory reduction for the active training. Implications are discussed. 10 references. (Author abstract modified)

185934 Quenzer, Linda F.; Feldman, Robert S.; Moore, John W. Psychology Dept., Tobin Hall, Univ. of Massachusetts, Amherst, MA 01002 **Toward a mechanism of the anti-aggression effects of chlordiazepoxide in rats.** Psychopharmacologia (Berlin). 34(1):81-94, 1974.

The mechanism of the antiaggression effects of chlordiazepoxide (CDP) was examined in rats. Rats were given CDP before testing in the Ulrich and Azrin shock induced aggression paradigm for 10 days. CDP significantly decreased shock induced aggression but fighting rates did not increase over the course of testing with the drug. Thus any tolerance to the general behavioral depressant effect of the drug either did not occur or the behavioral depression was not responsible for the reduction in aggression. Other rats were given no drug, caffeine and CDP, alone or in combination in a spontaneous activity test. CDP suppressed activity, caffeine increased activity and the two drugs in combination had antagonistic effects. The same drugs were used alone or in combination to measure their effects on shock induced aggression. CDP suppressed aggression, as did caffeine and the two drugs together had additive effects. It is concluded that CDP induced general behavioral depression was not responsible for suppression of aggression but more likely the property of CDP as a c-AMP phosphodiesterase is responsible for the antiaggression effect. 23 references. (Author abstract modified)

185954 Borberg, S. Sct. Hans Hospital, Dept. E, DK-4000 Roskilde, Denmark **Conditioning of amphetamine-induced behaviour in the albino rat.** Psychopharmacologia (Berlin). 34(3):191-198, 1974.

The behavior induced by amphetamine in rats was studied to determine if it is susceptible t the influence of stimulation in such a way that o conditioning could take place. Amphetamine was injected into 12 male albino rats every fourth to fifth day, 30 times per rat in all and behavior was recorded 10 to 31M in after injection. During the observation period four rats were electrostimulated when they did not demonstrate stereotype, which is well defined, constantly and spontaneous occurring amphetamine induced behavior. Four rats were stimulated when demonstrating stereotype and four rats acted as control group and were not stimulated. The behavior in the groups differed as follows: the stereotype group demonstrated a high percentage of stereotypy per experiment, the nonstereotypy group a low percentage, while the results of the control group lay between those of the stimulated groups. It is concluded that stereotypy can be subjected to conditioning. 4 references. (Author abstract modified)

185955 Gomer, Frank E.; Jakubczak, Leonard F. Washington Univ., St. Louis, MO 63130 **Dose-dependent selective facilitation of response-contingent light-onset behavior by d-amphetamine.** Psychopharmacologia (Berlin). 34(3):199-208, 1974.

The influence of d-amphetamine on the acquisition of light contingent bar-pressing was assessed in rats in a two lever operant task as a function of dose and incentive value of the sensory reinforcer. Relative to saline injected controls, amphetamine increased the probability of discriminated responding on the active reward bar at the 0.75 but not at the 2.5mg/kg dosage level. Only at the lower dose was the effect of incentive condition significant. It is concluded that low doses of amphetamine do not enhance all categories of behavior in the rat in a learning situation but selectively facilitate only those responses directed by the reinforcement contingencies. The poor performance observed for animals injected with the higher dosage in the experiment may have been due to the stimulated perseveration of stereotypic patterns which were incompatible with the task requirements. 34 references. (Author abstract)

185957 Owen, John E., Jr.; Campbell, James T. Lilly Research Laboratories, Eli Lilly and Co., Indianapolis, IN 46206 **Effects of methamphetamine on fixed-ratio responding of food satiated and food deprived rats.** Psychopharmacologia (Berlin). 34(3):223-232, 1974.

The effects of methamphetamine on fixed-ratio responding of food satiated and food deprived rats was examined. After the initial training of the lever pressing response for sweetened condensed milk, rats were put on different fixed-ratio (FR) schedules of reinforcement conditions of being food satiated and food deprived. Doses of methamphetamine were tested in these rats for effects on response rates. Response rates of the satiated rats at the higher FR requirements were slower than those of the deprived rats. At the doses of methamphetamine used, the satiated animals responded at slower than their control response rates and the deprived rats tended to respond faster than the control rates. 14 references. (Author abstract)

185958 Costall, B.; Naylor, R. J. Postgraduate School of Studies in Pharmacology, Univ. of Bradford, Bradford, Yorkshire BD7 1DP, England **On catalepsy and catatonia and the predictability of the catalepsy test for neuroleptic activity.** Psychopharmacologia (Berlin). 34(3):233-241, 1974.

In an attempt to differentiate the behavioral states in rats called catalepsy and catatonia, haloperidol and morphine were closely compared using drug interaction and brain lesion studies. Atropine abolished or reduced the effects of haloperidol, peromide and spiroxatrine but not morphine, while morphine and spiroxatrine were modified by nalorphine. The spiroxatrine effect was completely abolished by atropine and nalorphine combined. The cholinergic agent, spiro-(N'-methylpiperidyl-4') -N-ethylsuccinimide hydrogenfumarate, synergized with haloperidol, peromide and spiroxatrine but not with morphine. Lesions of the dopaminergic extrapyramidal and/or mesolimbic innervation, of the caudate - putamen, globus pallidus and nucleus amygdaloideus centralis each reduced or abolished haloperidol, peromide, and spiroxatrine catelepsy/catatonia. Morphine catatonia was only partially reduced by ablating the mesolimbic input and was potentiated by lesions destroying the extrapyramidal/ mesolimbic innervation, caudate - putamen and globus pallidus. Morphine catatonia was more susceptible to inhibition by the amygdaloid than the catalepsy/catatonia induced by the other agents tested. 12 references. (Author abstract modified)

185959 Lassen, J. Buus. Dept. of Pharmacology, A/S Ferrosan, Sydmarken 1-5, DK-2860 Soeborg, Denmark **The effect of p-chloroamphetamine on motility in rats after inhibition of monoamine synthesis, storage, uptake and receptor interaction.** Psychopharmacologia (Berlin). 34(3):243-254, 1974.

The effect of p-chloroamphetamine (PCA) on motility was investigated after s.c. injection to rats in a familiar cage. The doses one, two, five and 10mg/kg induced increasing hypermotility. PCA 1 and 2mg/kg produced various normal ehavioral items but 5 and 10mg/kg induced mainly b abnormal jerky locomotion and head movements. The effects of PCA 5mg/kg was investigated in rats treated s.c. with various drugs affecting central monoamines. Pretreatment with the serotonin (5-HT) synthesis inhibitor, d,l-p-chlorophenylalaninmethyl-ester (H 69/17), the tyrosinehydroxylase inhibitor, alpha-MT methylester, (H 44/68) twice and reserpine inhibited PCA hyperactivity. H 44/68 once and the dopamine beta-hydroxylase inhibitor bis-4(methyl-l-homopiperazinylthiocarbonyl) (disulphide) did not influence the effect of PCA. Simultaneous administration of impiramine, chlorimipramine, desipramine, amitriptyline, doxepine, chlorpromazine, haloperidol, spiramidl, and chlorpheniramine antgonized PCA hypermotility. Protriptyline, clozapine and benzotropine showed no PCA antagonism. Results indicate that 5-HT and dopamine release are involved in PCA hyperactivity and that 5-HT membrane blockers inhibit the uptake of PCA into brain 5-HT neurons thus preventing 5-HT release. 50 references. (Author abstract modified)

185960 Yokel, Robert A.; Pickens, Roy. Psychiatry Research Unit, Box 392 Mayo, Univ. of Minnesota, Minneapolis MN 55455 **Drug level of d- and l-amphetamine during intravenous self-administration.** Psychopharamacologia (Berlin). 34(3):255-264, 1974.

The relationship between responding and drug level in stimulant self-administration was examined in rats. Rats were allowed to self-administer dextro (d) and levo (l) isomers of amphetamine in various amounts for 6 hr/day. Total body level of drug was calculated at the time of responding for each drug injection. Body level of amphetamine initially increased and then decreased (0-2 hr) and thereafter remained relatively constant for the remainder of the experimental session (2-6 hr). During 2-6 hr of self-administration, calculated whole body levels of both d-amphetamine and l-amphetamine remained

relatively constant across injection doses. In another study blood was removed several times during 2-6 h at the time of responding for drug injection. Again no difference in blood level of 14C-amphetamine was found across a range of injection doses. 18 references. (Author abstract modified)

185961 Wauquier, A.; Niemegeers, C. J. E. Dept. of Pharmacology, Janssen Pharmaceutica, Research Laboratory, B-2350 Beerse, Belgium **Intracranial self-stimulation in rats as a function of various stimulus parameters: IV. influence of amphetamine on medial forebrain bundle stimulation with monopolar electrodes.** Psychopharmacologia (Berlin). 34(3):265-274, 1974.

The effects of various doses of amphetamine on self-stimulation in rats, with monopolar nichrome electrodes, implanted in the medial forebrain bundle at the level of the lateral hypothalamus, were studied. Six different stimulus parameter combinations (SPC) inducing different predictable response rates were used. Response stimulation as well as response inhibition were measured at the same dose levels in the same rats and during the same experimental session. At each dose level of amphetamine response stimulation was more pronounced than response depression. The response depression was dose related and the response stimulation reached a peak at 0.63mg/kg. The response depression was directly related and the response stimulation inversely related to the control response rate obtained with the different SPC's. It was assumed that amphetamine enhanced self-stimulation by lowering the threshold at the synaptic level and by increasing catecholamine release at neurons mediating motivational properties and reinforcement. Inhibition of the response at high doses of amphetamine could be attributed to nonspecific motor stimulation interfering with performance efficiency. 41 references. (Author abstract)

185997 McKenzie, G. M.; Sadof, M. Dept. of Pharmacology, Wellcome Research Laboratories, Burroughs Wellcome Co., 3030 Cornwallis Rd., Research Triangle Park, NC 27709 **Effects of morphine and chlorpromazine on apomorphine-induced stereotyped behaviour.** Journal of Pharmacy and Pharmacology (London). 26(4):280-282, 1974.

The effects of morphine sulphate and chlorpromazine pretreatments on apomorphine induced stereotyped behavior were evaluated in male Sprague Dawley rats. Chlorpromazine caused a marked reduction in mean behavioral scores. Higher doses of chlorpromazine completely blocked stereotypy. Morphine does not effectively antagonize, but rather potentiates, apomorphine induced stereotyped behavior especially at low doses of apomorphine. The present findings suggest that the interaction between chlorpromazine and apomorphine is competitive, possibly at dopaminergic sites. The results are consistent with the concept that chlorpromazine blocks dopamine receptors in the central nervous system. 12 references.

186164 Atrens, Dale M.; von Vietinghoff-Riesch, Francisca; Der-Karabetian, Aghop; Masliyah, Esther. Department of Psychology, University of Sydney, Sydney, Australia **Modulation of reward and aversion processes in the rat diencephalon by amphetamine.** American Journal of Physiology. 226(4):874-880, 1974.

The effects of amphetamine on reward - aversion processes at a variety of diencephalic loci were studied in 38 albino rats. The influence of amphetamine on performance for intracranial stimulation was investigated in a free operant situation, providing a rate independent index of reward along with a simple index of aversion. The data indicate that amphetamine specifically enhances reward at lateral, medial, and paraventricular hypothalamic sites. This enchancement was seen at several drug dose levels and stimulating current intensities. In a number of instances, amphetamine precipitated a change from essentially pure escape to reliable and permanent self-stimulation. It is concluded that the concurrent aversion data represent an entirely new aspect to amphetamine's involvement in reinforcement processes. Amphetamine's effects on the aversive component of intracranial stimulation ranged from significant increases to virtual elimination of aversion, depending on which longitudinal - autonomic zone of the hypothalamus was being stimulated. 31 references. (Journal abstract modified)

186368 Nielsen, I. Moller; Fjalland, B.; Pedersen, V.; Nymark, M. H. Lundbeck and Co., Ottiliavej 7-9, 2500 Copenhagen-Valby, Denmark **Pharmacology of neuroleptics upon repeated administration.** Psychopharmacologia (Berlin). 34(2):95-104, 1974.

The development of tolerance, defined as a reduction in pharmacological potency, was studied in various experimental models following repeated administration of neuroleptic drugs to rats, mice and dogs. Tolerance developed in all models involving stereotyped behavior induced by central dopaminergic stimulation, where no tolerance developed to the cataleptogenic effect and the inhibition of conditioned avoidance reaction. Tolerance development was dependent on pretreatment dose and length of pretreatment period. Once developed, tolerance persisted for a considerable time, particularly in rats and dogs. Possible mechanisms by which tolerance could develop include: 1) increased turnover of dopamine, leading to larger quanta of transmitter being released by the indirect sympathomimetic amine, or 2) increased receptor sensitivity following the prolonged receptor blockade. 17 references. Author abstract modified)

186369 Fjalland, B.; Nielsen, I. Moller. H. Lundbeck & Co., Ottiliavej 7-9, 2500 Copenhagen-Valby, Denmark **Enhancement of methylphenidate-induced stereotypies by repeated administration of neuroleptics.** Psychopharmacologia (Berlin). 34(2):105-109, 1974.

The intensity of methylphenidate induced gnaw compulsion was investigated in haloperidol tolerant mice and in normal mice. In the withdrawal phase after repeated administration of haloperidol (1.25mg/kg p.o./day, 5 days), methylphenidate caused a significant increase in stereotyped gnawing as compared to the effect in normal mice. It is proposed that the mechanism behind this increase in response to methylphenidate could be increased receptor sensitivity. 20 references. (Author abstract)

186370 Fjalland, B.; Nielsen, I. Moller. Dept. of Pharmacology, H. Lundbeck and Co., Ottiliauej 7-9, DK-2500, Copenhagen-Valby, Denmark **Methylphenidate antagonism of haloperidol, interaction with cholinergic and anticholinergic drugs.** Psychopharmacologia (Berlin). 34(2):111-118, 1974.

The methylphenidate antagonistic effect of haloperidol was investigated in normal and haloperidol tolerant mice under the influence of cholinergic and anticholinergic treatment. Physostigmine increased the potency of haloperidol against stereotypies induced by methylphenidate, whereas scopolamine reduced the effect of haloperidol. The effect of haloperidol was influenced both in nonpretreated mice and in haloperidol pretreated mice. It is concluded that a cholinergic dopaminergic balance is important for the antagonistic effect of a neuroleptic agent against methylphenidate induced gnaw-

ing compulsion in normal mice and mice which have become tolerant to neuroleptics. 16 references. (Author abstract modified)

186371 Christensen, A. V.; Nielsen, I. Moller. H. Lundbeck and Co., Ottiliavej 7-9, DK-2500, Copenhagen-Valby, Denmark **Influence of flupenthixol and flupenthixol-decanoate on methylphenidate and apomorphine-induced compulsive gnawing in mice.** Psychopharmacologia (Berlin). 34(2):119-126, 1974.

The effects of flupenthixol and flupenthixol decanoate on methylphenidate and apomorphine induced compulsive gnawing in mice were examined. The influence of both substances on gnawing disappeared 2 days after administration. Influence of flupenthixol and flupenthixol decanoate on apomorphine induced behavior was followed for 12 days, and apomorphine induced gnawing was seen on the days on which the methylphenidate antagonistic effect had subsided. The apomorphine induced compulsive gnawing seen in flupenthixol and flupenthixol decanoate pretreated animals could be antagonized by additional small doses of flupenthixol given two hours before apomorphine. The interference of the neuroleptic drugs with dopaminergic receptors is discussed. 13 references. (Author abstract modified)

186372 Ksir, Charles J., Jr. Dept. of Psychology, P.O. Box 3415, University of Wyoming, Laramie, WY 82070 **Scopolamine effects on two-trial delayed-response performance in the rat.** Psychopharmacologia (Berlin). 34(2):127-134, 1974.

A two trial procedure was used to examine the importance of stimulus type, presence or absence of the stimuli at the time of choice and time since presentation of the stimuli in determining the effects of scopolamine. Some rats were required to switch response levers on trial two to the incorrect trial one lever, whereas others were required to operate the same lever for both trials. Two sets of trial one stimuli were employed for different rats. Scopolamine reduced choice accuracy more in the presence of one set of trial one stimuli than for the other set. The reduction of accuracy under scopolamine was greater when rats were required to switch on trial two than for the stay condition. Presence versus absence of the stimuli had an inconsistent influence on drug effect; and there was no interaction between length of absence of the stimuli and scopolamine induced decreases in accuracy, thus precluding an interpretation that scopolamine disrupts memory processes. 12 references. (Author abstract modified)

186373 Holtzman, Stephen G. Dept. of Pharmacology, Emory Universtiy, Atlanta, GA 30322 **Behavioral effects of profadol in the rat.** Psychopharmacologia (Berlin). 34(2):135-142, 1974.

The effects of profadol, an analgesic with mixed agonist and antagonist properties, were evaluated on continuous avoidance responding and locomotor activity in the rat. Profadol was tested alone and concomitantly with 8mg/kg of naloxone. Profadol had a biphasic effect on avoidance response, increasing it at from .5-8 mg/kg and decreasing it at 32mg/kg. Naloxone blocked both the rate increasing and the rate decreasing effects of profadol on avoidance responding. Locomotor activity was unaffected by .5-64mg/kg of profadol alone, but was increased when profadol and naloxone were administered together. Findings extend the dual action hypothesis for morphine to a partial morphine agonist and provide further evidence that the behavioral activity of narcotic antagonists can be evaluated in the rat in an objective and quantitative manner. 22 references. (Author abstract modified)

186374 Senault, B. Laboratoire Le Brun, 41 bis, bd. Anatole-France, F-93300 Aubervilliers, France **/Brain amines and apomorphine-induced intraspecific aggressive behavior in the rat./** Amines cerebrales et comportement d'agressivite intraspecifique induit par l'apomorphine chez le rat. Psychopharmacologia (Berlin). 34(2):143-154, 1974.

The etiology of apomophine induced aggressive behavior and inhibition of such behavior were studied. In rats sensitive to apomorphine induced agression, similar, but less pronounced aggressive reactions were induced by ET-495, a specific stimulant of dopaminergic receptors, and to a slight extent by L-Dopa, whereas clonidine was ineffective. Aggressiveness was nearly completely inhibited by phenoxybenzamine, only partially by DDC, 5-HTP, and FLA 63. In rats not sensitive to the action of apomorphine, simultaneous administration of clonidine and apomorphine induced aggressive reactions, as did a combination of clonidine and ET-495. Findings suggest that aggressive behavior induced by apomorphine might result from a stimulation of dopaminergic receptors, stimulation that would itself induce the setting of noradrenergic structures. 42 references. (Author abstract modified)

186567 Ferraro, Douglas P.; Gluck, John P.; Morrow, Charles W. 176 Psychology Hall, University of New Mexico, Albuquerque, NM 87131 **Temporally-related stimulus properties of delta9-tetrahydrocannabinol in monkeys.** Psychopharmacologia (Berlin). 35(4):305-316, 1974.

In a study of the temporally related stimulus properties of delta9-tetrahydrocannabinol (THC), a two choice operant discrimination procedure was used to train three monkeys to respond differentially between a fixed dose of THC and the drug vehicle alone. During the acquisition of the drug discrimination, both drug and vehicle alone were administered orally 2.5h prior to the experimental session. The drug stimulus time course was than tested by administering either the same dose of THC or the vehicle alone from 0.5to 16.5h before the session. Varying administration time had no effect on the established discrimination during vehicle alone test sessions. However, orderly time related generalization gradients were obtained around the drug administration time used during discrimination training. 24 references. (Author abstract)

186568 Kelfer, Deborah A.; Rosen, Alexander J. Department of Psychology, Purdue University at Indianapolis, 1201 East 38th St., Indianapolis, IN 46205 **Effects of methamphetamine, pipradrol, and methylphenidate on instrumental conditioning and spontaneous motor activity in the immature rat.** Psychopharmacologia (Berlin). 35(4):317-326, 1974.

The effects of methamphetamine, pipradrol, and methylphenidate on instrumental conditioning and spontaneous activity were compared in the rat. All those drugs impaired the acquisition and performance of a simple alternation light on - light off instrumental response in weanling rats. High drug doses drastically reduced differential response (DR) rates and markedly elevated spontaneous motor activity (SMA). Low drug doses depressed DR asymptotes and slightly increased SMA. These findings with young rats are comparable to those with adult rats and question the usefulness of the immature rat as a model for the effects of stimulants in children. 7 references. (Author abstract)

186571 Kmieciak-Kolada, Krystyna; Herman, Zbigniew S.; Slominska-Zurek, Jadwiga. Department of Pharmacology, Silesian School of Medicine, 41-808 Zabrze, Poland **Behavioural and biochemical effects of 6-hydroxydopa in rats.** Psychopharmacologia (Berlin). 35(4):341-352, 1974.

The influence of 6-hydroxydopa (6-HDP) injected into the lateral ventricles of rat brain on the behavior of animals was examined. The level of noradrenaline (NA), 5-hydroxytryptamine (5-HT) and 5-hydroxyindoleacetic acid (5-HIAA) in discrete areas of the brain was also measured. Immediately after 6-HDP injection, circling movements, convulsions, aggressive behavior, and stereotypic activity were seen. These components of behavior were most obvious during the first hour after injection of 6-HDP. Twenty min after administration of 6-HDP a decrease of the NA level but no changes in the 5-HT level in the brain cortex were seen. The same changes were observed 1 month after 6-HDP treatment. 6-HDP decreased the NA level in the brain cortex, cerebellum, mesencephalon and brain stem 5 days after treatment. 5-HT content was not changed and the 5-HIAA level was increased in the same brain areas. It is concluded that 6-HDP is a long acting potent depletor of NA in rat brain. 16 references. (Author abstract modified)

186573 Dudderidge, H. J.; Gray, Jeffery A. Department of Experimental Psychology, South Parks Road, Oxford OX1 3PS, England **Joint effects of sodium amylobarbitone and amphetamine sulphate on resistance to extinction of a rewarded running response in the rat.** Psychopharmacologia (Berlin). 35(4):365-370, 1974.

The joint effects of sodium amylobarbitone and amphetamine sulfate on resistance to extinction of a rewarded running response in the rat were examined. Male rats were trained to run in an alley for food reward on continuous reinforcement. During extinction they were divided into four equal groups and injected with either amphetamine sulphate, amylobarbitone sodium, both of these two drugs, or saline. Amylobarbitone significantly retarded extinction and amphetamine on its own had no effect on resistance to extinction. Amphetamine in combination with amylobarbitone, however, potentiated the effects of the latter. These results confirm previous findings of a more than additive effect on behavior of amphetamine and amylobarbitone in combination. It is suggested that the psychological states of fear and frustration share a common physiological substrate. 15 references. (Author abstract)

186576 Delbarre, Bernard; Schmitt, Henri. Fondamentales et Appliquees, 40, avenue du Recteur Pineau, 86000 Poitiers, France **Effects of clonidine and some alpha-adrenoreceptor blocking agents on avoidance conditioned reflexes in rats: their interactions and antagonism by atropine.** Psychopharmacologia (Berlin). 35(3):195-202, 1974.

The effects of clonidine and some alpha-adrenoceptor blocking agents on avoidance conditioned reflexes were examined in rats. Clonidine depressed avoidance conditioned reflexes in Long-Evans rats. Some alpha-adrenoceptor blocking agents piperoxan, tolazoline, phentolamine, dibenamine and phenoxybenzamine also depressed these reflexes. Yohimbine was found to have no significant effect. Atropine antagonized the depression of conditioned avoidance reflexes induced by alpha-adrenoceptor blocking agents as well as the depression produced by clonidine. Yohimbine reduced the depressing effects of clonidine on avoidance conditioned reflexes. In rats treated with piperoxan the effects of clonidine were reduced. In these rats the depression of conditioned reflexes was less than in rats treated with clonidine or piperoxan alone. These experiments suggest that clonidine depressed avoidance conditioned reflexes in rats by activating central alpha-adrenoceptors. It is proposed that alpha-adrenoceptor blocking agents might act as partial agonists. 22 references. (Author abstract)

186581 Poschel, B. P. H.; McCarthy, D. A.; Chen, Graham; Ensor, Charles R. Pharmacology Department, Parke, Davis and Company, 2800 Plymouth Road, Ann Arbor, MI 48106 **Pyrazapon (CI-683): a new antianxiety agent.** Psychopharmacologia (Berlin). 35(3):257-271, 1974.

Pyrazapon (CI-683), a new antianxiety agent is examined. Pyrazapon, a pyrazolodiazepinone, exerts strong disinhibitory effects on behavior in a variety of animal tests (ingestion of a novel food substance, conditioned conflict, hypothalamic self-stimulation). In tests for sedation, motor depression and ataxia, weak effects were seen relative to chlordiazepoxide and diazepam. Pyrazapon also shows considerable ability to protect against pentylenetetrazol induced convulsions in acute tests. However, much tolerance develops to this effect in the course of daily treatments. Tolerance does not develop, on the other hand, to the behavioral disinhibitory effect. No untoward pharmacodynamic effects were observed at doses several fold greater than those producing the principle pharmacologic effects. Pyrazapon may well be an effective antianxiety drug with very weak sedative side-effects. 14 references. (Author abstract)

186583 Liu, Yali; Braud, William G. Psychology Department, Albright College, Reading, PA 19530 **Modification of learning and memory in goldfish through the use of stimulant and depressant drugs.** Psychopharmacologia (Berlin). 35(2):99-112, 1974.

The effects of stimulants and depressants on learning and memory in goldfish were investigated. Avoidance performance in a two way, light cued shuttle task was significantly facilitated by intercranial injection of picrotoxin but significantly impaired by injection of sodium pentobarbital 5 min before 20 training trials were given. These drugs in the dosages used in the present study did not affect general activity of the fish. When identical doses of the drugs (along with saline controls) were given immediately after the first two of three 10 trial training sessions 48 h apart, avoidance performance during the second and third sessions was facilitated and impaired by the posttrial injections of the stimulant and depressant drugs respectively. It was found in an extended experiment that picrotoxin improved performance if injected 25 sec or 1h after each of two 10 trial training sessions, but not if injected after a 4h delay. These stimulant and depressant effects demonstrated in goldfish were interpreted in terms of their effects on memory consolidation processes. 17 references. (Author abstract modified)

186586 Corcoran, Michael E.; Amit, Zalman. Department of Psychiatry, University of British Columbia, Vancouver V6T 1W5, Canada **Reluctance of rats to drink hashish suspensions: free-choice and forced consumption, and the effects of hypothalamic stimulation.** Psychopharmacologia (Berlin). 35(2):129-147, 1974.

Free choice and forced consumption of hashish suspensions was studied in male Wistar rats who drank a concentrated aqueous suspension of hashish in the absence of alternative fluids for 30 days. The Ss rejected the drug when water was also made available. In another experiment rats given a choice between water and varying concentrations of hashish also rejected concentrated suspensions, but they appeared less reluctant to drink dilute concentrations. Neither a schedule of alternate day presentation of hashish nor forced electrical stimulation of lateral hypothalamus induced rats to increase their home cage intake of an aversive concentration of hashish, suggesting that the enhanced consumption of concentrated ethanol solutions obtained with these two procedures is not due to a

nonspecific tendency to ingest any drug offered. Thus rats are generally reluctant to self-administer hashish via the oral route, and their reluctance is not affected by several procedures which can increase their intake of other drugs. 29 references. (Author abstract)

186587 Papeschi, R.; Randrup, A.; Lal, S. Max-Planck-Institut fur Psychiatrie, Neuropharmakologie, Kraepelinstrasse 2, 8000 Munich 40, W. Germany **Effect of ECT on dopaminergic and noradrenergic mechanisms: I. Effect on the behavioural changes induced by reserpine, alpha-methyl-p-tyrosine or amphetamine.** Psychopharmacologia (Berlin). 35(2):149-158, 1974.

In a study of the effect of electroconvulsive shock (ECT) on dopaminergic and noradrenergic mechanisms, the preliminary application of one or 5-8 ECTs significantly increased the severity of the sedation and catalepsy induced by reserpine or alpha-methyl-p-tyrosine (AMT). ECTx7, prior to various doses of d-amphetamine, significantly depressed the locomotor stimulation and the rearing, and slightly antagonized the decrease of social interactions induced by this drug. No consistent effect was found on amphetamine induced stereotyped activity. Locomotor activity was already depressed in the ECT group before amphetamine. The results suggest that ECT cannot affect such spontaneous and drug induced behavior through an increased functional catecholamine turnover, but rather through a decreased flow of nerve impulses in catecholaminergic neuronal systems and/or through increased nonfunctional catecholamine turnover or other nonspecific neurological changes. 17 references. (Author abstract)

186588 Papeschi, R.; Randrup, A.; Munkvad, I. Max-Planck-Institut fur Psychiatrie, Neuropharmakologie Kraepelinstrasse 2, 8000 Munchen 40, W. Germany **Effect of ECT on dopaminergic and noradrenergic mechanisms: II. Effect on dopamine and noradrenaline concentrations and turnovers.** Psychopharmacologia (Berlin). 35(2):159-168, 1974.

The effects of electroconvulsive shock on dopaminergic and noradrenergic mechanisms were examined in rats. The preliminary daily application of electric convulsive shock (ECT) for 7 days to rats significantly retarded the depletion of dopamine (DA) and noradrenaline (NA) by alpha-methyl-p-tyrosine (AMT) and decreased the accumulation of homovanillic acid (HVA) by probenecid in the brain, when these drugs were injected 5 min after the last shock or sham shock. The steady state concentration of brain catecholamines was not changed by preliminary ECT, whereas that of HVA was increased. The preliminary application of ECT for 5 days did not significantly affect the depletion of catecholamines nor the increase of HVA in the brain by reserpine. When the ECT treated rats and the reserpine controls were pooled as a group, a significant negative correlation was found between the total brain concentration of DA and NA and the behavioral scores for sedation and catalepsy, while the scores were positively correlated with brain HVA. This finding supports the contentions that spontaneous behavior suppressed by AMT or reserpine is correlated with the concentration and turnover of total brain catecholamines and not with newly synthesized ones. Results suggest that sedation and catalepsy are due to the interference with noradrenergic and dopaminergic mechanisms in the brain. 21 references. (Author abstract modified)

186590 Bucci, Luigi; Bovet, Daniel. Laboratory of Psychobiology and Psychopharmacology, Via Reno 1, Rome, Italy **The effect of iproniazid and tranylcypromine studied with a dark-avoidance conditioned schedule.** Psychopharmacologia (Berlin). 35(2):179-188, 1974.

The effect of iproniazid and tranylcypromine were examined with a dark avoidance conditioned schedule in rats. Different groups of rats were first trained with a dark avoidance conditioned schedule of the shuttle box technique. Subsequently different doses of iproniazid and tranylcypromine were injected i.p. and their effects upon the levels of conditioning were measured according to a specific timetable, different for the two drugs. While iproniazid, at doses of 25.5and 100mg/kg almost always induced a decrease of the percentage of the conditioned responses, tranylcypromine, at doses of 2.5and 5mg/kg, caused a marked increase of the same, 5 h after its administration. Such percentage increase of the conditioned avoidance response seems to be temporally related to the marked increase of brain norepinephrine induced by this latter drug, also 5 h after its administration. A comparative study between tranylcypromine and d-amphetamine shows the advantages of this particular type of schedule to distinguish between different classes of central nervous system stimulating drugs. 19 references. (Author abstract modified)

186613 Wise, Roy A.; Dawson, Vivien. Department of Psychology, Center for Research on Drug Dependence, Sir George Williams University, Montreal 107, Quebec **Diazepam-induced eating and lever pressing for food in sated rats.** Journal of Comparative & Physiological Psychology. 86(5):930-941, 1974.

Diazepam induced eating and lever pressing for food in sated rats are reported. Diazepam produced vigorous eating but not drinking in sated rats. The effect was found with familiar food in both test box and home cage and during both day and night. Animals trained under food deprivation lever pressed for food but not water under diazepam; the rate of response was dose dependent. Diazepam motivated learning of lever pressing for food but not so well as did deprivation. Diazepam induced eating lasted 25-30 min and was terminated by feedback from eating, rather than by catabolism of the drug. Stomach loads of food but not of water inhibited the eating. These data indicate that diazepam has specific actions on hunger of food - satiety mechanisms. 27 references. (Author abstract)

186620 Glick, S. D.; Marsanico, R. G.; Greenstein, S. Bernstein Institue, Beth Israel Medical Center, 307 Second Avenue, New York, NY 10003 **Differential recovery of function following caudate, hippocampal, and septal lesions in mice.** Journal of Comparative & Physiological Psychology. 86(5):787-792, 1974.

Mice with bilateral caudate, hippocampal, or septal lesions were tested for passive avoidance learning at 1-2, 7-8, or 28-29 days after surgery. Although each lesion induced a comparable learning impairment at 1-2 days after surgery, time dependent recovery occurred only with caudate lesions. Although each lesion induced changes in sensitivity to d-amphetamine and scopolamine at 1-2 days after surgery, further time dependent variations in drug sensitivity occurred only with caudate lesions. The results suggest that normal acquisition of passive avoidance behavior is mediated by a critical septal - hippocampal system and another, perhaps redundant, system involving the caudate. Time dependent drug sensitivity changes following caudate lesions were consistent with a role of denervation supersensitivity in recovery of function. 14 references. (Author abstract)

186630 Walsh, J. Michael; Bachrach, Arthur J. Behavioral Sciences Department, Naval Medical Research Institute, Bethesda, MD 20014 **Adaptation to nitrogen narcosis manifested**

by timing behavior in the rat. Journal of Comparative & Physiological Psychology. 86(5):883-889, 1974.

Adaptation to nitrogen narcosis manifested by timing behavior in the rat is reported. Albino rats trained on a temporal discrimination task were exposed to hyperbaric conditions to investigate these phenomena. Initial exposures to a simulated depth of 200 ft. in a hyperbaric chamber resulted in marked disruptions of the temporal discrimination and significant decrements in performance. Repeated exposures gradually lessened decrements until performance under pressure was equivalent to baseline control rates. 14 references. (Author abstract)

186634 Breese, G. R.; Cooper, B. R.; Grant, L. D.; Smith, R. D. Department of Pharmacology, University of North Carolina School of Medicine, Chapel Hill, NC 27514 **Biochemical and behavioural alterations following 5, 6-dihydroxytryptamine administration into brain.** Neuropharmacology (Oxford). 13(3):177-187, 1974.

Biochemical and behavioral alterations following 5,6-dihydroxytryptamine (5,6-DHT) were examined in rat brain. Administration of 5,6-DHT intracisternally caused a prolonged reduction of brain serotonin with little effect on brain catecholamines. This effect was moderately potentiated by administering an additional dose of 5,6-DHT or pretreating animals with pargyline before injection of 5,6-DHT. Injections of 5,6-DHT into the raphe nuclei also caused reductions in brain serotonin, but caused severe tissue damage in some rats as well. 5,6-dihydroxytryptamine given intracisternally to 7-day-old neonatal rats produced only a 30% reduction of serotonin. Reduction of tryptophan hydroxylase activity following 5,6-DHT treatment supports the view that the depletion of brain serotonin may be the result of fiber degeneration. In spite of moderate effects of 5,6-DHT on brain serotonin, treatments caused behavioral alterations including enhanced muricide and facilitated acquisition of an active avoidance task. 27 references. (Author abstract)

186635 Thornburg, J. E.; Moore, K. E. Department of Pharmacology, Michigan State University, East Lansing, MI 48823 **A comparison of effects of apomorphine and ET495 on locomotor activity and circling behaviour in mice.** Neuropharmacology (Oxford). 13(3):189-197, 1974.

The effects of apomorphine and trivastal; 1-(3,4-(methylenedoxy)benzyl)-4(2-pyrimidyl)piperazine (ET495) on locomotor activity were compared to circling behavior in mice. In mice with 6-hydroxydopamine induced left striatal lesions, apomorphine and ET495 produced dose related contralateral circling behavior. Apomorphine was 30 times more potent than ET495 with respect to the dose required to elicit the half maximal rate of circling. ET495, however, had a markedly longer duration of action. In normal mice apomorphine stimulated locomotor activity, whereas ET495 depressed activity. Pretreatment with SKF-525A did not prevent ET495 induced depression. In contrast to its effects in mice, ET495 stimulated locomotor activity in rats. 25 references. (Author abstract)

186636 Davies, J. A.; Jackson, B.; Redfern, P. H. Department of Pharmacology, Welsh National School of Medicine, Heath Park, Cardiff CF4 4XW, England **The effect of amantadine, L-dopa, (+)-amphetamine and apomorphine on the acquisition of the conditioned avoidance response.** Neuropharmacology (Oxford). 13(3):199-204, 1974.

The effect of amantadine HCl, L-DOPA methyl ester, (+)-amphetamine sulphate and apomorphine HCl on the acquisition of a conditioned avoidance response (CAR) was studied in rats. Pretrial injection of all four drugs produced a significant dose dependent improvement in acquisition at low doses. In higher doses, all four drugs decreased the rate of acquisition of the CAR. Amantadine, which produced the most significant improvement in acquisition when injected before each trial, also produced a significant improvement following posttrial injection. None of the drugs had any effect on retrieval of the CAR when given to animals previously trained to a 90% criterion. The significance of these results in terms of the involvement of brain dopamine in learning and memory mechanisms is discussed. 23 references. (Author abstract)

186637 Cox, T.; Tye, N. Department of Psychology, University of Nottingham, Nottingham, NG7 2RD, England **Effects of physostigmine on the maintenance of discrimination behaviour in rats.** Neuropharmacology (Oxford). 13(3):205-210, 1974.

The behavioral effects of physostigmine were studied using the maintenance of various discrimination behaviors in rats. Small doses of the drug brought about an improvement in performance on all the tasks studied, while a larger dose brought about an impairment of performance. Increasing the discriminative difficulty of the tasks brought about a shift in the dose response curve. The effects of physostigmine were reversed by atropine but not by methyl atropine. Postsession administration of the cholinesterase inhibitor had little effect on behavior. It was argued that this drug affected central cholinergic mechanisms of response inhibition, but did not interfere with memory processes. 16 references. (Author abstract)

186638 Ellis, K. O.; Carpenter, J. F. Pharmacology Section, Norwich Pharmaceutical Company, Norwich, NY 13815 **A comparative study of dantrolene sodium and other skeletal muscle relaxants with the Straub tail mouse.** Neuropharmacology (Oxford). 13(3):211-214, 1974.

Dantrolene sodium was compared to other skeletal muscle relaxants in the Straub tail mouse. Male mice treated subcutaneously with morphine sulphate developed a Straub tail reaction within 15 min. The elevated tail has been used as a model of contracted muscle for studying the effects of a variety of drugs which induce muscle relaxation. The effective Straub tail antagonists (dantrolene sodium, diazepam, chlordiazepoxide, neuromuscular blocking agents and local anaesthetics) were further compared for their ability to cause loss of righting reflex and acute toxicity. Effects on motor coordination were also determined for the two benzodiazepines and dantrolene sodium. Dantrolene sodium was more specific than diazepam, chlordiazepoxide, neuromuscular blocking agents, and local anesthetics in relaxing the Straub tail without causing acute toxicity, loss of righting reflex or motor incoordination. 8 references. (Author abstract)

186645 Ferraro, Douglas P.; Gluck, John P. 176 Psychology Hall, University of New Mexico, Albuquerque, NM 87131 **Effects of oral delta9-tetrahydrocannabinol on operant reinforcement schedule performance in rats.** Pharmacology (Basel). 11(2):65-69, 1974.

The effects of oral delta9-tetrahydrocannabinol (THC) on operant reinforcement schedule performance in rate were examined. Eight rats were trained to bar-press for water reinforcement under a variable interval 60 sec operant schedule. Nine acute oral administrations of THC in amounts ranging from 0.25-64mg/kg, produced dose related effects on responding; overall response rate increased at lower doses, while higher doses produced a suppression of responding and a cor-

responding loss of reinforcements. It was concluded that oral THC has a biphasic effect on operant behavior in rats which closely resembles that obtained with intraperitoneal drug administrations. 11 references. (Author abstract)

186667 Winter, J. C. Capen Hall, State University of New York, Buffalo, NY 14214 **The effects of 3,4-dimethoxyphenylethylamine in rats trained with mescaline as a discriminative stimulus.** Journal of Pharmacology and Experimental Therapeutics. 189(3):741-747,1974.

The ability of 3,4-dimethoxyphenylethylamine (DMPEA), a nonhallucinogen, to substitute for mescaline in animals previously trained with mescaline and saline was examined. Subjects were first trained on a variable interval schedule of positive reinforcement. Two treatment conditions, mescaline hydrochloride and saline, were then assigned to each animal. One treatment was SD, the stimulus in whose presence responses were reinforced, and the other treatment was S delta, the stimulus in whose presence no responses were reinforced. Administration of a range of doses of DMPEA to subjects in which saline functioned as SD and mescaline as S delta revealed the DMPEA was equivalent to the training dose of mescaline. The same doses, when tested in subjects in which mescaline was SD, did not result in responding appropriate for the mescaline condition. Subsequently, direct comparisons of DMPEA and mescaline were made by substituting DMPEA for saline:1) in subjects previously trained with mescaline and saline; and 2) in a second group which had previously received neither drugs nor behavioral training. Discriminated responding developed rapidly in both groups. The present results suggest the DMPEA cannot substitute for mescaline in a discriminative task and that comparable doses of the two drugs are discriminable in rats. 28 references. (Author abstract modified)

186670 Tseng, L.-F.; Loh, H. H. Department of Pharmacology, University of California, San Francisco Medical Center, San Francisco, CA 94143 **Significance of dopamine receptor activity in dl-p-methoxyamphetamine- and d-amphetamine-induced locomotor activity.** Journal of Pharmacology and Experimental Therapeutics. 189(3):717-724, 1974.

The effects of apomorphine, bulbocapnine and haloperidol on dl-p-methoxyamphetamine (PMA) induced d-amphetamine induced locomotor activites were studied in mice and rats. Small doses of PMA or of apomorphine given alone did not increase the locomotor activity. When both PMA and apomorphine were injected into mice or rats, a marked increase in locomotor activity was induced. The increased locomotor activity caused by a high dose of PMA or by small doses of d-amphetamine was blocked effectively by bulbocapnine or haloperidol. PMA, even in high doses, did not induce stereotyped behavior. d-Amphetamine, but not PMA, antagonized bulbocapnine induced catalepsy in mice. The results are consistent with the biochemical findings that PMA is as effective as d-amphetamine in causing the release of norepinephrine from central norepinephrine containing neurons, but is much less effective than d-amphetamine in causing the release of dopamine from central dopamine containing neurons. The results indicate that activation of both central norepinephrine and dopamine receptors is important for the increased locomotor activity after the administration of d-amphetamine. 34 references. (Author abstract)

186683 Sodersten, Per; Larsson, Knut. Department of Psychology, University of Goteborg, Box 14094, S-400 20 Goteborg 14, Sweden **Lordosis behavior in castrated male mice treated with estradiol benzoate or testosterone propionate in combination with an estrogen antagonist, MER-25, an in intact male rats.** Hormones & Behavior. 5(1):13-18, 1974.

The effects of estradiol benzoate, testosterone propionak, and MER-25 on lordosis behavior in castrated male rats and in intact rats were examined Lordosis behavior could be elicited by manual stimulation in castrated male rats after treatment with estradiol benzoate or testosterone propionate. The effect was antagonized by treatment with the estrogen antagonist MER-25. Prolonged treatment with testosterone propionate resulted in display of male as well as female sexual behavior. Eleven of 32 intact male rats and 22 or 27 other intact males displayed lordosis in response to manual stimulation without hormonal treatment. Seven intact males which showed lordosis without hormone treatment were injected with MER-25 and lordosis was abolished in six cases. The results suggest that estrogen is involved in the regulation of lordosis behavior in TP treated and intact male rats. 24 references. (Author abstract)

186686 Feder, H. H.; Morin, L. P. Institute of Animal Behavior, Rutgers University, Newark, NJ 07102 **Suppression of lordosis in guinea pigs by ethamoxy-triphetol (MER-25) given at long intervals (36-46 hr) after estradiol benzoate treatment.** Hormones & Behavior. 5(1):63-71, 1974.

The supression of lordosis in guinea pigs by ethamoxytriphetol (MER-25) given at long intervals (34-46 hr) after estradiol benzoate (EB) treatment is reported. Ovariectomized guinea pigs were given EB followed 40 hr later by progesterone (P). This treatment activated lordosis in almost 100% of animals. Administration of the antiestrogen MER-25 between 2 hr before and 6 hr after EB treatment did not cause a significant decline in proportion of animals displaying lordosis, but did not cause a decrease in length of time the lordosis position was held (maximum lordosis, sec). In contrast, 13/14 animals given MER-25 at 2 hr before and 2 hr after P and 8/10 animals given MER-25 simultaneously with and 2 hr after P, failed to show lordosis. Administration of supplementary EB at around the time of P injection, partially alleviated these behavior blocking effects of MER-25. When MER-25 was given 2-6 hr after administration of P there was a significant decrease in duration of heat. These results suggest that in addition to its early triggering effects, estrogen has important maintenance effects which determine the character of heat in guinea pigs. 16 references. (Author abstract modified)

186691 Sodersten, Per. Department of Psychology, University of Goteborg, Box 14 094, S-400 20 Goteborg 14, Sweden **Effects of an estrogen antagonist, MER-25, on mounting behavior and lordosis behavior in the female rat.** Hormones & Behavior. 5(1):111-121, 1974.

The effects of an estrogen antagonist, MER-25, on mounting behavior and lordosis behavior were examined in the female rat. Four daily injections of 20mg ethamoxytriphetol, MER-25, to intact female rats with regular 4 day estrous cycles inhibited lordosis behavior, but had no inhibitory effect on mounting behavior. Ten mg/day of MER-25 for 9 days partially antagonized the stimulatory effect of estradiol benzoate on lordosis behavior in ovariectomized female rats, but had no inhibitory effect upon mounting behavior. MER-25 stimulated the display of mounting behavior in ovariectomized female rats. No effects of MER-25 treatment comparable to those of testosterone propionate on testicular, seminal vesicle, or ventral prostate weights of intact male rats or on seminal vesicle or ventral prostate weights of castrated male rats were observed. The results show that MER-25 acts differently upon various estrogen sensitive behaviors in the female rat. 7 references. (Author abstract)

186692 Graeff, F. G. Department of Pharmacology, Faculty of Medicine, Ribeirao Preto, Sao Paulo, Brazil **Tryptamine antagonists and punished behavior.** Journal of Pharmacology and Experimental Therapeutics. 189(2):344-350, 1974.

The dose effect relationships of two tryptamine antagonists, methysergide and cyproheptadine, on lever pressing behavior of rats were determined. A concurrent fixed-interval 1 minute water, fixed-ratio five electric shock punishment schedule was used. Since cyproheptadine shows antihistaminic as well as antimuscarinic actions, dose response curves for atropine and the three antihistaminic drugs, diphenhydramine, pyrilamine and HS-592, on punished responding were determined. The effects of selected doses of the minor tranquilizers, chlordiazepoxide and pentobarbital on punished performance were also measured. Appropriate doses of methysergide, cyproheptadine, chlordiazepoxide, pentobarbital and atropine increased response rates suppressed by punishment. Small, but measurable, increases in mean response rate (maximum 136% of control) followed the administration of 1 to 10mg/kg of atropine. In contrast, the three antihistaminics caused only rate decreasing effects on punished responding. These results suggest that tryptamine antagonists increase response rates suppressed by punishment by interfering with a tryptaminergic mechanism in brain involved in behavioral inhibition. 37 references. (Author abstract modified)

186700 Cools, A. R. Department of Pharmacology, University of Nijmegen, Nijmegen, Netherlands **The transsynaptic relationship between dopamine and serotonin in the caudate nucleus of cats.** Psychopharmacologia (Berlin). 36(1):17-28, 1974.

In order to study the relationship between dopamine (DA) and serotonin (5-HT) mechanisms in the caudate nucleus of cats, a behavioral analysis was made of effects brought about by simultaneously or successively administered injections of DA, 5-HT, carbachol and some related compounds into the DA sensitive caput nuclei caudati rostromedialis (CRM area) and the 5-HT sensitive caput nuclei caudati anteroventralis (CAV area) in cats. The data reported here show that inhibition of the 5-HT activity in the CAV area abolishes the effects elicited by activation of the DA mechanism in the CRM area, and that inhibition of the DA mechanism in the CRM area does not influence the effects elicited by inhibition of the 5-HT activity in the CAV area. The study shows that inhibition of the cholinergic mechanism in the CAV area abolishes the effects elicited by the activation of the DA mechanism in the CRM area. The experiments reveal that inhibition of the 5-HT mechanism in the CAV area abolishes the effects elicited by activation of the cholinergic mechanism in the CAV area, whereas inhibition of the cholinergic mechanism does not affect the effects elicited by activation of the 5-HT mechanism in this area. A model by which these neurotransmitter systems might operate is proposed. 28 references. (Author abstract)

186702 Bell, David S.; Kirkby, Robert J.; Preston, Alan C. Psychiatric Research Unit, Callan Park Hospital, Rozelle, N.S.W. 2039, Australia **Tolerance to the hyperactivating effects of methylamphetamine.** Psychopharmacologia (Berlin). 36(1):41-47, 1974.

The development of tolerance to the hyperactivating effects of methylamphetamine was studied in the laboratory rat. The results of Experiment I indicated that tolerance did develop. In Experiment II these indications were confirmed and the time course of tolerance was plotted. It appeared that the development of tolerance could be divided into two phases: an initial period of about one week during which activity increased, possibly due to accumulation of the drug or a metabolite, and a later period lasting about 6 weeks during which activity gradually fell to the first day of drug administration. 21 references. (Author abstract)

186703 Vasko, Michael R.; Lutz, Michael P.; Domino, Edward F. Department of Pharmacology, University of Michigan, Ann Arbor, MI **Structure activity relations of some indolealkylamines in comparison to phenethylamines on motor activity and acquisition of avoidance behavior.** Psychopharmacologia (Berlin). 36(1):49-58, 1974.

The structure activity relationships (SAR) of various known hallucinogenic and nonhallucinogenic indolealkylamine and phenethylamine derivatives were compared on two different behaviors: mouse locomotor activity and acquisition of one way avoidance behavior in the rat. Certain parallels were observed between the two classes of compounds. Alpha-methyl substituted derivatives of the indoles and phenethylamines increased dramatically psychomotor stimulant effects. Acquisition of one way avoidance behavior was reduced by the more potent hallucinogens and psychomotor stimulants of both classes. Pargyline pretreatment enhanced the psychomotor stimulant effects of all of the compounds tested except 5-hydroxytryptamine (5-HT), d-amphetamine, mescaline and lysergic acid diethylamide (LSD-25). 19 references. (Author abstract)

186704 Sara, Susan J.; David-Remacle, Michele. Center for Experimental and Comparative Psychology, University of Louvain, 3040 Pellenberg, Belgium **Recovery from electroconvulsive shock-induced amnesia by exposure to the training environment: pharmacological enhancement by Piracetam.** Psychopharmacologia (Berlin). 36(1):59-66, 1974.

In a study of recovery from electroconvulsive shock induced amnesia by exposure to the training environment, rats were trained at a one trial passive avoidance task and were then submitted to electroconvulsive shock or sham electroconvulsive shock. Before training the animals received 100mg/kg of Piracetam, a nontoxic, nonsedative, nonanaleptic drug which has been shown to be active in learning and memory. Control animals received water. Other groups were treated with Piracetam 30 min before the retention test, 24 h after training. Results indicated that the product was active during the retrieval phase of memory, but it did not offer protection from ECS induced amnesia, when administered before training. The results are discussed in relation to other findings with the same drug. 26 references. (Author abstract)

186705 Castellano, Claudio. Laboratorio di Psicobiologia e Psicofarmacologia, C.N.R. 1, via Reno I-00198, Roma, Italy **Cocaine, pemoline and amphetamine on learning and retention of a discrimination test in mice.** Psychopharmacologia (Berlin). 36(1):67-76, 1974.

Cocaine, pemoline and amphetamine were tested on mice trained to swim toward the light (L procedure) or toward the dark (D procedure) in a Y water maze, in pretrial and posttrial experiments. In the pretrial experiments no differences between controls and drugged animals appeared under the L Procedure (ceiling effect), while in the D Procedure all drugs induced a clear facilitation; however, while a state dependent effect was evident for cocaine no state dependency appeared following pemoline and amphetamine administration. In the posttrial experiments (D Procedure), cocaine did not affect retention, while the other two drugs induced clear facilitating effects on the consolidation processes. No effect on the performance of trained animals in either procedures appeared following pemoline administration. 17 references. (Author abstract)

187066 Branch, Marc N.; Gollub, Lewis R. Department of Psychology, University of Florida, Gainesville, FL 32611 **A detailed analysis of the effects of d-amphetamine on behavior under fixed-interval schedules.** Journal of the Experimental Analysis of Behavior. 21(3):519-539, 1974.

The effects of d-amphetamine on behavior under fixed-interval schedules were studied in pigeons. Ss were exposed to fixed-interval schedules of food reinforcement with duration of 300 sec, 100 sec, or 40 sec. A range of doses of d-amphetamine was administered to each pigeon, and the resulting behavior was analyzed at several levels of detail. Average rates in different portions of the intervals predicted the magnitude of the drug's effect but a finer analysis showed that average rates did not adequately characterize the behavior in some parts of the intervals. The probability of responding in different parts of an interval without drug was also a good predictor of the magnitude of the effect of d-amphetamine, and at the same time as more descriptive of the interval to interval performance. Analyses of the control performance indicated that responding in individual intervals could be described as consisting of two parts: a very low, or zero, rate at the beginning of the interval followed by an abrupt transition to a slightly, but reliably, positively accelerated rate maintained until reinforcement. 21 references. (Author abstract)

187119 Neuburg, Janet; Thut, Paul D. College of Medicine, Arizona Medical Center, Tucson, AZ **Comparison of the locomotor stimulant mechanisms of action of d-amphetamine and d-amphetamine plus l-dopa: possible involvement of serotonin.** Biological Psychiatry. 8(2):139-150, 1974.

The locomotor stimulant mechanisms of the action of d-amphetamine and d-amphetamine plus l-dopa in mice were compared. Male mice were pretreated with Ro.4-4602 and treated with doses of d-amphetamine or with d-amphetamine plus doses of l-dopa. Spontaneous motor activity was enhanced in a dose related manner by these treatments. Haloperidol, a dopamine receptor blocking agent, reduced the ability of low doses of the agonist to enhance motor activity. p-Chlorophenylalanine, an inhibitor of serotonin synthesis, enhanced the agonist effects of low doses of l-dopa and d-amphetamine. The response to high doses of l-dopa and d-amphetamine was not significantly affected by either pretreatment. The results were interpreted to suggest an agonist effect of dopamine and an antagonist effect of serotonin on spontaneous motor activity. 41 references. (Author abstract)

187129 Strahilevitz, Meir; Kelly, Kenneth A.; Tsui, Paulus T.; Sehon, Alec H. Department of Psychiatry, Washington University, St. Louis, MO 63104 **Blocking of the effect of a delta1-tetrahydrocannabinol (delta1-THC) on spontaneous motor activity in the rat by immunization with a protein conjugate of delta1-THC.** Life Sciences (Oxford). 14(10):1975-1989, 1974.

The blocking of the effect of delta7-tetrahydrocannabinol (THC) on spontaneous motor activity in the rat by immunization with a protein conjugate of THC is reported. Rats actively immunized with porcine gamma globulinhemisuccinate-THC showed higher spontaneous motor activity after intraperitoneal administration of THC at a dose of 10mg/kg than did rats immunized with a control antigen, porcine gamma globulinhemisuccinate-phenol. The capacity to neutralize the effect of THC was found to depend on the degree of immunization; thus, the difference in mean spontaneous motor activity after injection of THC was significant in rats which had received five injections of the immunogen over a period of 86 days, and not in those which had received only two injections over a period of 34 days. It is suggested that the observed neutralization of the effect of THC in animals receiving multiple injections of protein conjugates of THC may be due to the binding of the drug by anti-THC antibodies thus preventing THC from reaching drug receptor sites. 19 references. (Author abstract modified)

05 TOXICOLOGY AND SIDE EFFECTS

182442 Stolk, J. M. Dartmouth Medical School, Hanover, NH **Rubidium salts -- animal toxicity studies.** Psychopharmacology Bulletin. 10(1):32-38, 1974.

Animal toxicity studies on rubidium salts were reported at a workshop entitled 'Rubidium: Safety and Potential as an Antidepressant,' which was sponsored by the National Institute of Mental Health in November 1972. Data from the Japanese subacute toxicity study in rats, an investigation of acute lethality in mice, and subacute toxicity studies in dogs are presented. Findings indicate the need for more comprehensive and systematic experiments focusing on rubidium's potential for causing anatomic destruction, physiological dysfunction in the urinary tract, hematologic abnormalities, gastrointestinal irritation and lesions, and pulmonary lesions. 2 references.

184585 Luers, H.; Vogel, E.; Obe, G. Institut fur Genetik, Freie Universitat Berlin, Arnimallee 5-7, D-1 Berlin 33, Germany **Mutagenicity experiments with the tranquillizer meprobamate in Drosophila melanogaster and in human leukocyte chromosomes in vitro.** Experientia (Basel). 30(3):310-312, 1974.

Mutagenicity experiments with the tranquilizer meprobamate in Drosophila melanogaster in vivo and in human leukocyte chromosomes in vitro are reported. For determination of recessive x-chromosome lethals in drospohila, the Basc technique was used. Berlin males were fed or injected with a solution of the drug and later mated with a virgin female. Germ cell stages of different age of spermatogenesis, including spermatogonia, were tested separately. Results with the Basc technique did not show any elevation of the recessive lethal frequency over the baseline. Experiments were also performed using the blood of a normal healthy man to which water solutions of meprobamate were added. No chromosome breaking ability of meprobamate on human leukocy es in vitro was noted. t 10 references.

186476 Chang, Louis W.; Yamaguchi, Seiya; Dudley, Alden W., Jr. Department of Pathology, University of Wisconsin, Madison, WI **Neurological changes in cats following long-term diet of mercury contaminated tuna.** Acta Neuropathologica (Berlin). 27(2):171-176, 1974.

Young kittens of both sexes fed daily with mercury contaminated tuna were studied to detect neurological changes. Neurological disturbances similar to those in Minamata disease or in experimental mercury intoxication were observed after 7-11 months. Microscopic examination revealed degenerations of the granular layer and some Purkinje neurons in the cerebellum. Neuronal necrosis was also observed in the cerebral cortex. The investigation suggest that fish containing 0.5ppm mercury may still be potentially hazardous to health when consumed in excessive amounts for prolonged periods of time. 30 references. (Author abstract)

187076 Al-Hachim, G. M.; Al-Baker, A. Instituut voor Veterinaire Farmacologie en Toxicologie, Rijksuniversiteit Utrecht, Netherlands **The prenatal effect of chloramphenicol on the postnatal development of mice.** Neuropharmacology (Oxford). 13(4):233-237, 1974.

In a study of the prenatal effect of chloramphenicol on the postnatal development of mice, five groups of eight pregnant albino mice, at the third stage of pregnancy were given chloramphenicol or distilled water. The drug or vehicle was given orally for 7 consecutive days. Conditioned avoidance response indicated that there were significant differences among treatments, days of treatment and animals within the treatments (as reflected in a reduction in learning ability for chloramphenicol treated offspring). Electroshock seizure threshold showed that there were differences among treatments (as reflected in an increase in brain seizure threshold for chloramphenicol treated offspring). The open field test showed significant differences among treatments and among animals within the treatments (as reflected in an increase in fright of chloramphenicol offspring). 16 references. (Author abstract modified)

06 METHODS DEVELOPMENT

182623 Masuda, Tetsuro. Department of Legal Medicine, Kumamoto University School of Medicine, Japan **Medicolegal studies on isolation and identification of hypnotics by thin layer chromatography (TLC): report 2 -- isolation and identification of hypnotics and tranquilizer in vivo.** Journal of the Kumamoto Medical Society (Kumamoto). 46(4):199-207, 1972.

The isolation and identification of three hypnotics and one tranquilizer: Luminal, Brovarin, Hyminal and Atraxin from the liver, stomach contents, blood and brain of rabbits by thin layer chromatography after oral administration of each of these drugs is discussed. The results are summarized. In the Stas-Otto method frequently used for extraction and purification, there was a failure to obtain satisfactory results. Curry's method, sodium tungstate precipitation and extraction with other solvents was found to be a suitable procedure for the extraction of Luminal, Brovarin and Atraxin from the organs. For the identification of three hypnotics and one tranquilizer by TLC, the most suitable solvent system and color reagents were used. 21 references. (Author abstract modified)

185749 Marcy, R.; Quermonne, M. A. Laboratoire de Pharmacodynamie, 1 rue Vaubenard, 14032 Caen-Cedex, France **An improved method for studying the psychogalvanic reaction in mice and its inhibition by psycholeptic drugs. Comparison with the effects of other pharmacological agents.** Psychopharmacologia (Berlin). 34(4):335-349, 1974.

An apparatus and a quantitative method for studying the spontaneous palmar conductivity (SPC) and the psychogalvanic reaction (PGR) in mice are described. Several psycholeptic (neuroleptics, tranquilizers, hypnotics) were tested. In order to assess the specificity of the method, several other pharmacological agents (muscle relaxants, neuromuscular blocking agents, anticholinergics) were tested. A comparison of the active doses of these various products on SPC, PGR, prehension and traction reflexes showed that psycholeptics and especially neuroleptics and tranquilizers inhibit PGR at low dosages. The method was found to be valid for screening and studying psycholeptic drugs. 35 references. (Author abstract modified)

186376 MacPhail, Robert C.; Gollub, Lewis R. Lab. of Psychopharmacology, University of Maryland, College Park, MD **Independence of the effects of d-amphetamine and food deprivation or body weight on the food consumption of rats.** Psychopharmacologia (Berlin). 34(2):163-172, 1974.

Two experiments examined the combined effects of absolute doses (milligrams per rat) of d-amphetamine with either food deprivation or body weight on the food consumption of rats. Increasing doses of d-amphetamine and decreasing levels of food deprivation both decreased food consumption, but the effects of the two variables were additive with nonsignificant interaction. Increasing does of d-amphetamine and decreased body weights decreased food consumption, and the combined effects of these two variables were additive. The lack of an interaction between dose and differing body weights indicates that the generally accepted mode of administering d-amphetamine, as milligrams per kilogram of body weight, does not equate rats of differing body weights. 18 references. (Author abstract modified)

186377 Tomasi, Laura; Bianchi, Camillo. Laboratori Ricerche, Societa Prodotti Antibiotici, Milano, Italy **A new recording apparatus for measurement of locomotor activity of mice. Experimental observations on its use.** Psychopharmacologia (Berlin). 34(2):155-162, 1974.

The reliability of a new apparatus for evaluation of the effects of some central stimulant and depressant drugs on the locomotor activity of mice was investigated. The locomotor activity of normal mice, mice treated with chlorpromazine, diazepam, methylphenidate, d-amphetamine and pemoline was determined. The depressant effect of chlorpromazine and diazepam, the stimulant effect of amphetamine, methylphenidate and pemoline were dose related. The stimulant properties of amphetamine were seen only in mice in which the normal orienting response had worn off. Results indicate that the recorder is reliable. 15 references. (Author abstract modified)

186589 Krieglstein, J.; Stock, R. Pharmakologisches Institut der Universitat, D-6500 Mainz, Obere Zahlbacher Str. 67, Germany **The isolated perfused rat brain as a model for studying drugs acting on the CNS.** Psychopharmacologia (Berlin). 35(2):169-177, 1974.

An isolated perfused brain preparation is regarded as offering some important advantages over intact animals or tissue slices for studying drug effects on the central nervous system (CNS). Investigations are presented proving the viability of the isolated perfused rat brain for more than 7 hours and its suitability for studies on cerebral metabolism. Until now this preparation has been successfully used for pharmacological investigations concerning the drug effects on cerebral energy metabolism, on the electroencephalogram and on the biogenic amines in the CNS. The results further demonstrate that the use of an isolated perfused rat brain affords the possibility of clarifying pharmacological problems which has not been possible using conventional methods. 33 references. (Author abstract)

187132 Bloom, Floyd E. NIMH, St. Elizabeth Hospital, Washington, DC 20032 **To spritz or not to spritz: the doubtful value of aimless iontophoresis.** Life Sciences (Oxford). 14(10):1819-1834, 1974.

The innovative technique of microiontrophoresis is evaluated. With the method, drugs can be applied in minute quantities directly into the immediate extracellular environment of single neurons. This procedure not only eliminates many of the diffusional and enzymatic barriers restricting the access of drugs to neuronal receptors, but even more importantly, it restricts the number of neurons which could initiate the response. However, the micromethod of drug delivery does not merely make the site of possible drug actions on central neurons easier to interpret. Despite an immense amount of data and frequent reviews the significance of the responses

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observed with microiontophoresis remains unclear because those who accumulate the data frequently disagree on the reproducibility of the observations and their meaning. 118 references. (Author abstract modified)

CLINICAL PSYCHOPHARMACOLOGY

07 EARLY CLINICAL DRUG TRIALS

183190 Bobon, Jean; Bourdouxhe, Suzanne; Breulet, M.; Mormont, C.; Parent, M. Dept. of Psychiatry. University of Liege, Rue Saint-Laurent 58, B-4000, Liege, Belgium **/Double-blind clinical trial of Noveril and of Noveril TR (Noveril 240mg)./** Essai clinique a double insu du Noveril simple et du Noveril TR (Noveril 240mg). Acta Psychiatrica Beligica (Bruxelles). 72(6):633-652, 1972.

Twenty depressed inpatients received dibenzepine hydrochloride (Noveril) and sustained rebase dibenzepine (Noveril TR) to confirm the antidepressant properties of the drug and to compare the action of both forms. A double-blind crossover procedure during a 6 week period was applied. Positive results were obtained for 10 patients; seven had received Noveril TR first, then Noveril; three received the reverse sequence. The main therapeutic results consist of psychomotor activation. Differences of action between the two forms are not yet understood, but it appears that Noveril TR is preferable to Noveril at the waxing stage of therapy. It is suggested that the administration of Noveril TR once a day constitutes a definite therapeutic asset. 6 references. (Author abstract modified)

184617 Boucsein, W.; Janke, W. Psychologisches Institut II der Universitat, 4 Dusseldorf, Moorenstr, 5, BRD **/Psychological experimention on the effects of propiramfumarate and promethazine under normal and stress conditions./** Experimentalpsychologische Untersuchungen zur Wirkung von Propiramfumarat Promethazin unter Normal- und Stressbedingungen. Arzneimittel-Forschung(Aulendorf). 24(4a): 675-693, 1974.

The effects of propiramfumarate and promethazine were assessed under normal and stress conditions. N-(1-methyl-2-piperidino-ethyl)-N-(2-pyridyl)-propionamide-fumarate (propiramfumarate, Bay 4503) was tested in a double-blind study in comparison with promethazine and placebo. The three substances were administered in single doses to healthy volunteers and investigated for their psychic effect. The volunteers participated in 192 5h sittings, half of them under stress and the other half under normal conditions. Particular attention was given to the subjective feeling of activation, general state of well-being, subjectively experienced motorical excitation, time of reaction, psychomotoric quickness and accuracy, concentration, and verbal fluency. Results are summarized in tabular form. 32 references. (Journal abstract modified)

184965 Delaunay, J.; Guibert, S. Service de Psychotherapie, C.-H. La Rochelle, France **/The use of oral droperidol in psychiatric therapy./** Utilisation du droperidol per os en therapeutique psychiatrique. Annales Medico Psychologiques (Paris). 1(2):277-282, 1974.

A brief history of Droperidol, its chemistry and effects are summarized. It is used in anesthesiology as an operatory premedication agent as well as an preoperatory medication agent in association with an analgesic, and as a sedative in certain tests. The effects of Droperidol on a mixed diagnostic group of 29 females and 21 males between the ages of 16 and 74 years is described. It is shown that 66% of the patients treated showed net benfits. The drug was most useful in psychotics as a sedative, sedating excessive motoricity and reducing anxiety. Side-effects are minimal. Different dosages and methods of administration are taken into account for different types of treatments. 8 references.

08 DRUG TRIALS IN SCHIZOPHRENIA

182524 Houlihan, John Patrick. University of California, Los Angeles, CA **Word recognition of schizophrenics as a function of phenothiazine level and autonomic responsivity. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 73-1703 HC$10.00 MF$4.00 141 p.

The visual word recognition performance of 23 schizophrenic Ss was analyzed in terms of four patient variables: premorbid adjustment, paranoid status, phenothiazine level and autonomic responsivity. There was a significant interaction effect of Paranoid Status and Phenothiazine Level on the accuracy of Anxiety word recognition responses. Nonparanoid Ss receiving low levels of phenothiazine medication showed an increase in adaptation to the accurate recognition of affectively charged stimuli over repeated presentations, while Nonparanoid Ss receiving high levels of phenothiazine medication showed a decrease over trials in their ability to accurately recognize such stimuli. Differences in mean HR response were related to word recognition accuracy. For poor Premorbid Ss, increasing dosages of phenothiazine were associated with a tranquilizing effect as reflected in autonomic measures. For Good Premorbid Ss increasing phenothiazine levels were associated with an alerting autonomic pattern. (Journal abstract modified)

182581 Suk, Jae Ho. Department of Neuropsychiatry, Sacred Heart Hospital, College of Medicine, Chung Ang University, Seoul, Korea **The use of tranquilizing drugs in cases of schizophrenia.** Official Journal of Research Institute of Medical Science of Korea (Seoul). 5(4):37-39, 1973.

Tranquilizing drugs used in shizophrenia, with emphasis on their pharmacological actions, clinical usage, and side-effects are discussed. Neuroleptics in particular are discussed in great detail. Generally, neuroleptics do not cause schizophrenics to sleep, but with their action primarily in the subcartial area, they reduce psychiatric symptoms and sometimes even extrapyramidal effects. Detailed clinical data are reported. 5 references.

183195 Kudo, Yoshio. Dept. of Psychiatry, Osaka Keisatsu Hospital, Tennoji-Ku, Osaka, Japan **A double-blind comparison of pimozide with carpipramine in schizophrenic patients.** Acta Psychiatrica Belgica(Bruxelles). 72(6):685-697, 1972.

The effects and characteristics of pimozide are compared to those of carpipramine by studying the signifcance of pharmacotherapy in rehabilitation of schizophrenic patients. A double-blind, matched-pair method of testing over an 8 week period is used. The schizophrenic rating scale for doctors (Keio method) is applied as a means of rating effectiveness. Global judgement and sequential analysis fail to show significant differences between pimozide and carpipramine tested in therapeutic effectiveness. Results indicate that pimozide is more effective against disturbances of contact, social adjustment, social ability and social interest, consequently a better rehabilitation of schizophrenic patients. (Author abstract modified)

183196 Frangos, E. no address **Clinical observations on the use of pimozide in the treatment of chronic schizophrenics.** Acta Psychiatrica Belgica (Bruxelles). 72(6):698-707, 1972.

The usefulness, tolerance and method of therapeutic action of pimozide are discussed along with an evaluation of the possibility of substituting other neuroleptics in long-term maintenance treatment. Thirty chronic schizophrenics using other neuroleptics not providing satisfactory results were tested. Evaluation of results based on clinical criteria shows 19 patients with satisfactory improvement, nine with no change, and two deteriorating. Results indicate that pimozide is devoid of toxicity. Pimozide is concluded to be a specific drug combining motivating activity with an antihallucinatory and antidelusive effect while being free from any significant undesirable effects. (Author abstract modified)

183275 Polizos, Polizoes; Englehardt, David M.; Hoffman, Stanley P.; Waizer, Jonas. Dept. of Psychiatry, State University of New York, Downstate Medical Center, Brooklyn, NY 11203 **Neurological consequences of psychotropic drug withdrawal in schizophrenic children.** Journal of Autism and Childhood Schizophrenia. 3(3):247-253, 1973.

A preliminary study involving 34 schizophrenic children, 6 to 12 years of age, who were carefully observed following discontinuation of active neuroleptic treatment to ascertain the clinical effects of drug withdrawal is reported. The children had been on maintenance therapy for periods of 6 to 15 months. Five neuroleptics were involved: fluphenazine, haloperidol, thioridazine, trifluoperazine, and thiothixene. All but two children suffered massive clinical relapse within 1 to 2 weeks after drug withdrawal. Fourteen of the children exhibited neurological withdrawal emergent symptoms (WES) characterized by involuntary movements and ataxia. In half the children the WES remitted spontaneously. In the remainder, symptoms disappeared within 2 weeks of resumption of active treatment with another neuroleptic. The findings are discussed in relation to the syndrome of tardive dyskinesia observed in adult schizophrenics. 6 references. (Author abstract)

183629 Thetford, Paul E.; Spohn, Herbert E.; Everds, Joseph P. Dept. of Research, Menninger Foundation, Topeka, KS **Psychophysiological patterns of response in schizophrenia.** Journal of Nervous and Mental Disease. 158(2):104-114, 1974.

Psychophysiological patterns of response in schizophrenia were examined. Schizophrenic subgroups (paranoid vs. nonparanoid), (acute vs. chronic), (poor vs. good premorbids) did not differ on heartrate (HR) and skin conductance (SC). Paranoids showed significantly higher muscle tension (EMG) than nonparanoids, and there were no subgroup differences on blood pulse volume (BPV). Under phenothiazine medication patients showed lower SC and higher HR than normals, but after drug withdrawal patients showed both high SC and high HR. Correlations between the four psychophysiological measures provided little evidence for arousal as a unitary concept, and correcting for background variables by stepwise regression analysis did not modify the evidence for arousal. Analysis of coefficients of concordance, based on autonomic lability scores, showed that drugged schizophrenics were physiologically less sensitive to changes in the procedure than normals. 20 references. (Author abstract)

183683 Tsutsul'kovskaya, M. Ya.; Minsker, E. I.; Panteleyeva, G. P.; Mazursky, M. B.; Pekunova, L. G.; Lukanina, S. K. Moscow Psychiatric Clinical Hospital No.1 imeni P. P. Kashechenko, Moscow **/Features of the therapeutic effect of fluphenazine decanoate in schizophrenia./** K voprosu ob osobennostyakh terapevticheskogo deystivya flyufenazin-dekanoata (moditen-depo) pri schizofrenii. Zhurnal Nevropatologii i Psikhiatrii imeni S.S. Korsakova (Moskva). 73(5):753-758, 1973.

The features of the therapeutic effect of fluphenazine decanote in schizophrenia are considered. Dosages ranged from 12.5- 100mg every 2 to 5 weeks. The content of fluphenazine and its oxidized forms in the blood was measured using a spectrofluometer. In patients with a relatively stable condition and fragmental positive disorders such as obsessional rudimental hallucinatory and substuporous states, the fluphenazine decanoate had a greater effect than other psychotropic drugs. 11 references. (Journal abstract modified)

183955 Planas, Pedro; Arranz, Tomas. Institutos Psiquiatricos de San Baudilio de Llobregat, Barcelona **/Clinical study on the effects of thiothixene in hospitalized psychotic patients./** Estudio clinico del tiotixeno en enfermos psicoticos hospitalizados. Neurologia, Psiquiatria y Ciencias Afines (Madrid). 1(2):359-363, 1972.

The results of treating 25 male and 21 female patients hospitalized with chronic schizophrenia with thiothixene are tabulated. Most patients had been ill for many years and had long histories of hospitalization and were regarded as difficult cases. The antipsychotic activity of the drug, a thioanthene derivative, marketed as Navane by Pfizer, is evidenced in the form of inhibition of patients suffering from chronic schizophrenia. Patients, upon treatment, show better contact with the environment, improvement in motor behavior, and cooperativeness. The effect appears to be favorable in facilitating the integration of patients into work therapy and rehabilitation programs. 11 references. (Journal abstract modified)

183957 Lopez-Ibor Alino, J. M. Avenida Nueva Zelanda, 78, Puerto de Hierro-Madrid-35 **/On the dynamics and treatment of the tendency of schizophrenic psychosis to become chronic./** Sobre la dinamica y el tratamiento de la tendencia a la encronizacion de las psicosis esquizofrenicas. Neurologia, Psiquiatria y Ciencias Afines (Madrid). 1(2):377-388, 1972.

The factors leading to the evolution of chronic schizophrenic psychosis, such as age, constitutional makeup, and former personality are discussed. The manner in which chronicity sets in is described. Treatment is discussed to include the use of time release neuroleptics. Results are tabulated and charted. Best results are shown to have been obtained from the use of pipothiazine, which, in addition to its action over an extended period of time, has shown little evidence of damaging side-effects. The problem of how to treat insidious and progressive types of the disease, those clinically more malignant, is not yet solved, and optimism is not yet in evidence. Nevertheless the retarding neuroleptics have opened up a new frontier and have added a new dimension to treating the problem. 18 references.

184977 Wijsenbeek, H.; Steiner, M.; Goldberg, S. C. Gehah Psychiatric Dept., P.O.B. 72, Petah Tikvah, Israel **Trifluoperazine: a comparison between regular and high doses.** Psychopharmacologia (Berlin). 36(2):147-150, 1974.

A comparison between regular and high doses of trifluoperazine (TR-60mg and TR-600mg) was made on 26 newly admitted schizophrenics with acute psychotic symptoms. Eleven received the regular dose of the drug (TR-60mg) and 15 received the high dose (TR-600mg). Treatment duration

was 6 weeks. Psychiatric evaluations were done by means of Patient Personal Data Inventory, Brief Psychiatric Rating Scale, Inpatient Multidimensional Psychiatric Scale, Digit Symbol Test, Continuous Scanning, Side Effects, and Extrapyramidal Status. Almost all patients from both groups generally improved from the beginning to the end of the study, but the results provide no support for the contention that very high doses of TR are more effective than regular doses. 4 references. (Author abstract)

185005 McClelland, H. A.; Blessed, G.; Bhate, S.; Ali, N.; Clarke, P. A. St. Nicholas, Gosforth, Newcastle upon tyne, NE3 3XT, England **The abrupt withdrawal of antiparkinsonian drugs in schizophrenic patients.** British Journal of Pyschiatry (London). 124:151-159, 1974.

The abrupt withdrawal of antiparkinsonian drugs in schizophrenic patients was studied in a blind controlled trial using 99 patients on oral phenothiazine and depot phenothiazines. Only two out of 50 patients (4%) developed marked extrapyramidal symptoms within 4 weeks of withdrawal of their antiparkinson drugs. It is considered that two have later deteriorated clinically. A statistically significant increase in a mild degree of plastic rigidity was noted in the antiparkinson drug withdrawal groups, but no clinically apparent discomfort was observed in these patients. The occurrence of minor forms of extrapyramidal symptoms throughout the trial in all patients is noted and discussed. The implication of these findings, which confirm previous American studies, is that for the great majority of patients who have been on antiparkinson drugs for over 3 months, these drugs are unnecessary and can be withdrawn without disadvantage. Discontinuation whenever practicable is recommended. 18 references. (Author abstract modified)

185194 Trueman, H. R.; Valentine, M. G. Glenside Day Hospital, Bristol BS16 1DD, England **Flupenthixol decanoate in schizophrenia.** British Journal of Psychiatry (London). 124:58-59, 1974.

The antidepressant action of flupenthixol decanoate was tested in an uncontrolled trial with 19 outpatients and three inpatients selected on the basis of apathy depression, a poor response to other medication and, apart from two cases, a schizophrenic diagnosis. The total symptom score for the group of 14 patients who completed the trial fell progressively with each injection. It is concluded that flupenthixol decanoate depot injections are of value in the treatment of schizophrenic patients, particularly those who are apathetic, withdrawn or depressed. 5 references.

185213 Haneda, Tadashi. Tomobe Hospital, Ibaragi Prefecture, Japan **On the clinical effect of fluphenazine enanthate in outpatient schizophrenics.** Clinical Psychiatry (Tokyo). 15(8):898-899, 1973.

The clinical effect of fluphenazine enathate (FE) in schizophrenia was investigated. FE was experimentally administered in dosages of 12.5mg every 2 weeks. Results of intramuscular administration of FE as a supplementary drug are recorded. Subjects included: 1) patients hospitalized for periods from 5 to 10 years; 2) patients whose onset was recent and who were hospitalized frequently the previous year; and 3) outpatients who had never been hospitalized. Other drugs given to patients are detailed. Results of FE administration and various side-effects are reported.

185877 Sheppard, Charles; Moan, Eugene; Beyel, Virginia; Fracchia, John; Merlis, Sidney. Research Division, Central Islip State Hospital, Central Islip, NY **Comparative survey of psychiatrists' treatment preferences: California and New York.** Comprehensive Psychiatry. 15(3):213-223, 1974.

A questionnaire describing the clinical course of an acute paranoid schizophrenic was sent to psychiatrists in New York and California to evaluate the novelty of and the relationship of polypharmacy to chronicity. Data from 312 New York and 107 California respondents indicated a statistically similar preference for polypharmacy at first contact with the patient. As drug treatment became ineffective, respondents significantly increased their preference for drug combinations. On the patient's third hospital admission, more than half of the respondents preferred a combination of psychotropic drugs. Preference for polypharmacy is replaced by maxipharmacy as symptoms resist treatment. 6 references. (Author abstract)

186081 Kirov, K. no address **/Maintenance treatment of schizophrenia in the light of prognosis oriented diagnosis./** Podd'rzhashchoto Lekuvane na endogennite psikhozi v svetilinata na prognoznata diagnostika. Nevrologiya, Psikhiatriya i Nevrokhirurgiya (Sofia). 12(2):93-97, 1973.

Maintenance treatment of schizophrenia was studied in the light of prognosis oriented diagnosis. It is felt that in the majority of schizophrenic patients maintenance drug treatment is unnecessary. Prognosis oriented diagnosis of endogenous psychoses is an important factor in the decision to maintain a patient on continuous medication. It is noted that recurrent or nonproductive nuclear schizophrenic processes do not require supportive drug treatment. The major indication for drug maintenance is schizophrenia of the shift - progredient type or chronic forms. 19 references. (Journal abstract modified)

186288 Morritt, C. Lynfield Mount Hospital, Yorkshire, England **Long-acting phenothiazines and schizophrenia.** Nursing Mirror and Midwives Journal (London). 138(4):57-59, 1974.

The effect of long-acting phenothiazines on schizophrenia is discussed. Fluphenazine decanoate (Modecate) has been found effective for 23 days, with a reported lower incidence of extrapyramidal reactions. Of the over 200 patients receiving the drug, 183 received their injections at the Modecate clinic, 21 at the day hospital, and 37 in the community. After an initial period of stabilization, the patient was seen by the consultant psychiatrist on every other visit. It was found that patient readmission to hospital was significantly lowered with the Modecate treatment regime. This resulted in considerably lower hospital costs. Although finance is an important aspect of long-term therapy, the main purpose is to ensure continuous phenothiazine medication in schizophrenics responding to this group of drugs and to allow the patient to remain in the community and in many cases return to employment. 2 references.

186565 Fyro, Bengt; Wode-Helgodt, Birgitta; Borg, Stefan; Sedvall, Goran. Department of Pharmacology, Karolinska Institutet, S-104 01 Stockholm 60, Sweden **The effect of chlorpromazine on homovanillic acid levels in cerebrospinal fluid of schizophrenic patients.** Psychopharmacologia (Berlin). 35(4):287-294, 1974.

A mass fragmentometric method was used for determination of homovanillic acid levels in cerebrospinal fluid of acutely admitted schizophrenic patients. Spinal puncture was performed before and 12 days following the beginning of chlorpromazine treatment. The level of homovanillic acid in cerebrospinal fluid before treatment was significantly higher in women than in men. Chlorpromazine treatment resulted on the average in a more than twofold elevation of the homovanillic acid level in

cerebrospinal fluid. There were marked individual differences in the effect. The results are compatible with the view that therapeutic doses of chlorpromazine accelerate brain dopamine synthesis in man. 25 references. (Author abstract modified)

186994 McCabe, O. Lee. Maryland Psychiatric Research Center, Baltimore, MD 21228 **Psychedelic (LSD) psychotherapy: a case report.** Psychotherapy: Theory, Research and Practice. 11(1):2-10, 1974.

The technique of psychedelic peak psychotherapy, involving LSD induced peak experiences, is examined in the case of a patient with pseudoneurotic schizophrenia. The patient background is cited, psychological testing and psychotherapy described, and drug administrations noted. Followup evaluations are reported. Posttreatment psychometric assessment indicates dramatic alteration in the patient's clinical condition, although the study does not differentiate between the effect of the LSD versus the psychotherapy itself. 10 references.

187113 Cohen, Stephen M.; Nichols, Anna; Wyatt, Richard; Pollin, William. Department of Psychiatry, University of Vermont, School of Medicine, Burlington, VT **The administration of methionine to chronic schizophrenic patients: a review of ten studies.** Biological Psychiatry. 8(2):209-225, 1974.

A review of 10 studies of the administration of methionine to chronic schizophrenics is presented. The presence of neurologic symptoms and signs, including features most frequently associated with organic brain syndrome, was consistently found. In light of the findings of these ten studies, with special reference to the high frequency of symptoms and signs of organic brain disorder and neurologic involvement, the administration of the methyl donor methionine to chronic schizophrenic patients does not seem to be a model for, or explanation of, schizophrenia. It seems beyond dispute, however, that the administration of a physiologic amino acid, methionine, has profound pharmacologic effects on the mood, perception, and central nervous system of patients with a diagnosis of schizophrenia. 22 references. (Author abstract modified)

187255 Simpson, George M.; Varga, Ervin; Reiss, Martin; Cooper, Thomas B.; Bergner, Per-Erik E.; Lee, J. Hillary. Research Center, Rockland State Hospital, Orangeburg, NY **Bioequivalency of generic and brand-named chlorpromazine.** Clinical Pharmacology and Therapeutics. 15(6):631-641, 1974.

Fifty chronic schizophrenic patients were included in a double-blind, crossover clinical and metabolite comparison of generic and Thorazine brand forms of chlorpromazine. Improvement was similar in quality and degree with the two compounds; there was no difference in frequency or severity of side-effects or in incidence of laboratory abnormalities. Side-effects consisted mainly of extrapyramidal reactions, drowsiness, and hypotension; the most serious were grand mal seizures that occured in two patients, one on each compound. Weight changes and neuroleptic threshold were similar. Kinetic studies were carried out during the drug free intervals. Chlorpromazine, chlorpromazine nor, and chlorpromazine sulfoxide nor were measured over a 24 hour period. The characteristics of the mean curves were similar, although there were marked interindividual differences. The urinary recovery over the same period also demonstrated wide individual variability although the results from the same patients were similar. It is concluded that the two compounds are bioequivalent. 17 references. (Author abstract modified)

09 DRUG TRIALS IN AFFECTIVE DISORDERS

182430 Stack, John J. St. John of God Brothers, Child Psychiatric Services, 59, Orwell Road, Rathgar, Dublin 6, Ireland **Chemotherapy in childhood depression.** In: Annell, A., Depressive states in childhood and adolescence. Stockholm, Almqvist & Wiksell, 1972. 541 p. (p. 460-466).

At the Fourth Congress of the Union of European Pedopsychiatrists in Stockholm, August 30 - September 3, 1971, different types of childhood depression were analyzed as seen in a sample of patients in an outpatient clinic of a children's hospital. Out of 4500 patients referred over a 5 year period, 490 cases of depression were identified. Treatment with psychotropic drugs is described and the reactions of different types of depressive illness to chemotherapy are tabulated. The necessity for evaluation of the total family situation and for concomitant psychotherapy is stressed. Classification of the depression was according to two groups: 1) depression in preschool children, including hyperactivity, apathy, and somatic complaints; and 2) depressions in school age children, including simple depression, phobic or obsessional children with depressive reactions, mixed depressive states, and depressions associated with organic brain syndromes and psychotic states. Primary drugs used in treatment were the tricyclic antidepressants and monoamine oxidase inhibitors. 8 references. (Author abstract modified)

182433 Schou, Mogens. Psychopharmacology Research Unit, Statshospitalet, Dk-8240 Risskov, Denmark **Lithium in psychiatric therapy and prophylaxis. A review with special regard to its use in children.** In: Annell, A., Depressive states in childhood and adolescence. Stockholm, Almqvist & Wiksell, 1972. 541 p. (p. 479-487).

At the Fourth Congress of the Union of European Pedopsychiatrists in Stockholm, August 30 - September 3, 1971, the usefulness of lithium therapy in treating depression was briefly discussed, with stress on its outstanding results with adult patients and the implications of such success for treating children and adolescents. In adult psychiatry, lithium (administered as one of its salts) has proven particularly effective in treating mania and in the prophylaxis against further attacks of recurrent endogenous affective disorder. Experience with children and adolescents is still limited. There are, however, experiences which indicate that in a number of patients with undulating or periodic disturbances of mood and behavior maintenance, lithium treatment may exert a stabilizing and normalizing action of a type that is not seen with other drugs. The clinical features which characterize lithium responders among children have yet to be defined. Such treatment should be conducted under proper clinical and laboratory control and with dosage adjustment according to the lithium level in the blood. Use of the drug requires care but is usually not difficult. Children seem to tolerate it well. 14 references. (Author abstract modified)

182434 Gram, Lars F.; Rafaelsen, Ole J. Psychochemistry Institute, Rigshospitalet, Dk-2100 Copenhagen **Lithium treatment of psychotic children. A controlled clinical trial.** In: Annell, A., Depressive states in childhood and adolescence. Stockholm, Almqvist & Wiksell, 1972. 541 p. (p. 488-490).

At the Fourth Congress of the Union of European Pedopsychiatrists in Stockholm, August 30 - September 3, 1971, the effectiveness of lithium treatment of psychotic children, evaluated in a double-blind cross-over trial of 2 months duration, was discussed. A total of 18 Ss were treated with lithium or placebo substances. Seven children improved during

treatment and worsened after discontinuation of the drug. No specific symptoms were influenced. No patients became totally free of symptoms. (Author abstract modified)

182443 Fieve, R. R.; Meltzer, H. L. New York State Psychiatric Institute, New York, NY **Rubidium salts -- toxic effects in humans and clinical effects as an antidepressant drug.** Psychopharmacology Bulletin. 10(1):38-50, 1974.

Clinical trials using rubidium which were carried out on patients in an eight bed metabolic ward were reported at a workshop entitled 'Rubidium: Safety and Potential as an Antidepressant,' which was held at the National Institute of Mental Health in November 1972. Data from blood and urine studies are presented and clinical effects, including evidence of rebound depression after discontinuance, are reported. Findings on therapeutic dosage levels within the safety range are based on studies in dogs. 4 references.

182620 Kimura, Masasuke; Sugano, Hisanobu; Suehiro, Koji. Kyushu University, Japan **Treatment process of depression and changes in microvibration.** Clinical Electroencephalography (Osaka). 14(2):89-93, 1972.

Microvibration of 85 patients with various types of depression (endogenous, involutional melancholia, and depressive neurosis) was studied, with 31 patients out of the 85 treated with chlorimipramine or amitriptyline for 3 weeks and compared with changes in microvibration (MV) before and after treatment. The nontreated Ss served as controls to establish 'normal' MV for these depressive types. The MV data is summarized. An increase in Type N MV was significantly correlated with improvement in clinical symptoms. 17 references.

182765 Merskey, H.; Buhrich, N. National Hospitals for Nervous Diseases, Queen Square, London, W. C. 1., England **Is oxypertine an activating tranquillizer?** Postgraduate Medical Journal (Oxford). 48(Suppl 4):26-29, 1972.

The effects of oxypertine as a tranquilizer and antidepressant in 27 male and 24 female outpatients with fairly intractable anxiety and depression was examined in a symposium on the pharmacology and clinical use of oxypertine in anxiety held at Cambridge in 1972. Affective illness was chronic in almost all patients and a number of other treatments had already been tried. Oxypertine was usually added to the existing treatment of the patients, initially in a dose of one 10mg capsule t.d.s.,increasing to 20mg and, in the case of 10 patients, to 30mg or more. Monoamine oxidase inhibitors were not given simultaneously. No patient seemed worse, 25 were improved, and in 7 of these there was marked improvement. It is felt that in this resistant group of patients, oxypertine was an effective tranquilizing drug for anxiety. An energizing effect appeared in five cases, but was relatively transitory. Possible side-effects included a rise in serum transaminases in one patient suspected of having a liver disease; and in six patients, drowsiness or excessive sedation was noted with doses of 10mg or less. The mood elevating effect of oxypertine is of short duration with addiction an unlikely problem. Oxypertine is a viable alternative where benzodiazepines have been used without enough improvement, a brief trial with oxypertine may avert the use of antidepressants and it is an appropriate supplement to the tricyclic group. 11 references. (Author abstract modified)

182788 Agresti, E.; De Biase, G. Ospedali Neuropsichiatrici di Firenze, Firenze, Italy /**Phenomenological - existential study of phobic - obsessive syndromes treated with chlorimipramine.**/ Indagine fenomenologico-esistenziale in sindromi fobico-ossessive trattate con clorimipramina. Riv. Sper. di Freniatria e Med. Legale delle Alienazioni Ment. (Reggio). 97(1):130-146, 1973.

Results of oral treatment with chlorimipramine in 15 patients with phobic and obsessional syndromes are described. Two groups were distinguished from the phenomenological study: those patients whose existence is completely involved in the phobia, and those patients whose existence is only partially involved in the phobia. A relationship between therapy with chlorimipramine and the two group classifications seems to exist. There was no improvement in patients of the first group whereas results from patients in the second group varied between excellent and good. 14 references. (Journal abstract modified)

182791 Pinto, F.; Ferro, F. M.; D'Angeli, P. Clinica delle Malattie Nervose e Mentali dell'Universita Cattolica di Roma, Rome /**Clinical data and sociopsychiatric implications of outpatient treatment with long-term phenothiazines.**/ Il trattamento ambulatoriale con neurolettici deposito. Dati clinici ed implicanze sociopsichiatriche. Riv. Sper. di Freniatria e Med. Legale delle Alienazioni Ment. (Reggio). 97(1):174-191, 1973.

Clinical data and sociopsychiatric implications of outpatient treatment with long-term phenothiazines are reported. Forty three patients with varied psychoses received an average of 17.5mg of phenothiazine every 2 weeks, with a maximum dose of 50mg in 21 days. The drug was reduced in two thirds of the patients during the course of treatment. In three cases, temporary changes of hepatic liver functions were noticed with no direct relation to dosage or length of treatment. In other patients, an administration of benzexol controlled these symptoms. The role of the drug in modifying relations between the patient and the staff and the patient and his environment over a period of 12 months clinical trial are described. 20 references.

182902 Devred, Dominique. no address /**A clinical study of L-tetrahydropalmatine (c.200) in a neuropsychiatric clinic.**/ Etude clinique dans un service de neuro-psychiatrie de la L-tetrahydropalmatime ou C.200. Oise, France, Fitz-James, 1971.

The effects of L-tetrahydropalmatine (C.200), an alkaloid extracted from the tubercules of Stephania glabra, on 26 patients is described. The expected sedative and hypnotic effects thought to be produced by the drug did not appear; and in the case of grave psychotics an inverse reaction was noted manifesting itself in states of extreme agitation, violent reactions, and insomnia unaffected even by hypnotic barbiturates. A reoccurrence of the anguish and pain experienced in the early stages of the psychoses, a renewal of suicidal tendencies, and a reappearance of a delirious state were also noted. Good therapeutic results were obtained on patients who had not been ill for a long period. These last patients became more sociable and through regular therapy were ready to become a part of society once more. It was concluded that studies with C.200 be limited to patients who do not have a long history of illness so that eventual therapeutic evaluations may best be discerned.

183189 Bobon, Jean; Collard, Jackie. Dept. of Psychiatry, University of Liege Medical School, Liege, Belgium **Present treatment of manic states.** Acta Psychiatrica Belgica (Bruxelles). 72(6):617-632, 1972.

The treatment of typical manic states is discussed with an emphasis on the evolution of aims and methods of treatment for specific cases. Types of manic states are described and

their symptoms are listed for reference. Developments of psychopharmacology are noted along with specific drug applications of different neuroleptics. Therapies involving the use of droperidol, clotiapine, beneperidol, and other neuroleptics and rules for usage of these medicines are given. Other manic state therapies including sleep cure, electroconvulsive therapy, diencephalic irradiations, sociotherapy, psychotherapy, and relaxation techniques are evaluated. 20 references.

183194 Amery, W.; Boom, A. J.; Huisman, N. G.; Kuipers, H.; van der Wiel, H. J.; Reyntjens, A. Medical Research Dept., Janssen Pharmaceutica, B-2340 Beerse, Belgium **A series of multicentric pilot trials with pimozide in psychiatric practice: IV. Pimozide in the treatment of patients with paranoid symptomatology.** Acta Psychiatrica Belgica (Bruxelles). 72(6):677-684, 1972.

A multicentric trial evaluating the clinical potential of pimozide in patients with predominant paranoid symptomatology is presented. In the first stage of the study, 25 patients, with paranoid symptomatology, optimal individual daily dose of pimozide is determined. In the second stage, the daily dose is administered unchanged and results are assessed by means of psychiatric evaluation questionnaires. Results indicate that the optimal daily dose ranges from 2 to 9mg. Significant improvement is obtained in several items of the rating scale. Results show that side-effects are mild or absent. 7 references. (Author abstract modified)

183202 van Renynghe de Voxvrie, G. Korte Ridderstraat, 1, B-8000 Bruges, Belgium **/Are the IMAO outdated?/** Les IMAO sont-ils depasses? Acta Psychiatrica Belgica (Bruxelles). 72(6):767-788, 1972.

The value of monoamine oxidase inhibitors (MAOI) in the treatment of depression is discussed in light of tests on a large number of patients treated by MAOI (over 5,000 patients). It is suggested that if certain rules of drug administration are observed, MAOI will continue to be a useful therapeutic aid and it is felt that the danger of their use is greatly exaggerated. A great specifity of reaction to the MAOI for certain patients is found. Results suggest that it is not necessary to exhaust all other existing antidepressants before passing to MAOI. (Author abstract modified)

183234 Simpson, F. O. Wellcome Medical Research Institute, Dept. of Medicine, Univ. of Otago Medical School, P. O. Box 913, Dunedin, New Zealand **Hypertension and depression and their treatment.** Australian and New Zealand Journal of Psychiatry (Carlton, Australia). 7(3):133-137, 1973.

The treatments of hypertension and depression are reviewed. Depression is usually treated by pharmacological stimulation of adrenergic mechanisms, and hypertension by pharmacological damping of these mechanisms. The drugs in question act at much the same sites and can, in certain combinations, interact with each other. A literature review of antihypertensive drugs and depression includes comments on the use of reserpine, clonidine, propranolol and the adrenergic neurone blocking agents. The recognition of depression in hypertensive patients and the blood pressure problems in patients on antidepressant therapy are discussed. 50 references.

183361 Roy, J. Y.; Pinard, G.; Hillel, J.; Gagnon, M. A.; Tetreault, L. St.-Jean-de-Dieu Hospital, Research Unit, Montreal, Canada **/Comparative evaluation of dibencycladine (Ludiomil) and imipramine in psychotic depression./** Evaluation comparative de la dibencycladine (Ludiomil) et de l'imipramine chez le deprime psychotique. Intern. J. of Clinical Pharmacology, Therapy and Toxicology (Munchen). 7(1):54-61, 1973.

Dibencycladine (Ludiomil, Ciba), a dibenzobicyclo-octadiene, was compared to imipramine in the treatment of psychotic depression. A total of 46 patients started the 28 day double-blind evaluation. Six had to be excluded because they developed serious paranoid symptoms, and five withdrew due to drug reactions. Although both groups improved significantly in the Max Hamilton and N.O.S.I.E. scales, no significant difference was statistically demonstrated between the two drugs. It seems, however, that more adverse effects and those of a more serious nature appeared in the Ludiomil group. There was no statistical proof for this clincial impression due to the small number of patients studied. 9 references. (Author abstract)

183547 Dunleavy, Desmond L. F.; Oswald, Ian. Dept. of Psychiatry, Univ. of Nottingham, Nottingham, England **Phenelzine, mood response, and sleep.** Archives of General Psychiatry. 28(3):353-356, 1973.

Effects of phenelzine on REM sleep in 22 patients with endogenous depression were studied, relating the time course of mood change to the time course of the induced REM sleep change. A period of placebo administration preceded administration of 60, 75, or 90mg of phenelzine dihydrogen sulfate daily. Patient self-ratings of mood were employed and independent judges selected the date of onset of sustained mood improvement with at least three out of four in agreement for nine of the patients. In these nine depressed patients, restoration of normal mood coincided with the delayed abolition of the signs of REM sleep. 11 references. (Author abstract modified)

183648 Sovner, Robert D.; McHugh, Paul R. Boston State Hospital, 591 Morton St., Boston, MA 02124 **Lithium in the treatment of periodic catatonia: a case report.** Journal of Nervous and Mental Disease. 158(3):214-221, 1974.

A case of periodic catatonia is described in which cyclical changes in the blood urea nitrogen (BUN), blood pressure, and pulse rate were detected and found to be positively correlated with the patient's periodic episodes of catatonic behavior. Following the diagnostic study the patient was treated with lithium carbonate for 69 days. Although the drug did not influence the course of the illness, it did dissociate the periodic psychopathology from the metabolic concomitants, i.e.,the BUN remained stable, there was no adrenergic shift with relapse, and the previously positive correlations did not occur. This is a hitherto unreported effect of lithium. Possible mechanisms of actions are discussed. 11 references. (Author abstract)

184160 Post, Robert M.; Kotin, Joel; Goodwin, Frederick K. 3-West Clinical Research Unit, Adult Psychiatry Branch, NIMH, Bethesda, MD 20014 **The effects of cocaine on depressed patients.** American Journal of Psychiatry. 131(5):511-517, 1974.

Cocaine, administered orally to patients with endogenous depressive illness, did not consistently affect vital signs or depressive symptomatology, but it did decrease rapid eye movement sleep and total sleep time. When administered intravenously in the context of a therapeutic interview, cocaine caused large, rapid increase in pulse and blood pressure concomitant with profound mobilization of affect and tearfulness. Infusions that caused lesser changes in vital signs were associated with milder degrees of affective change and less

dysphoria. While cocaine was capable of eliciting positive affective change (such as calmness and elation) in depressed patients, affective flooding and dysphoric components were often admixed, indicating that cocaine's effect in this context could not be classified simply as antidepressant. 49 references. (Author abstract)

184652 van Praag, Herman M.; Korf, Jakob. Dept. of Biological Psychiatry, Psychiatric Univ. Clinic, Groningen, Holland, the Netherlands **5-Hydroxytryptophan as an antidepressant: the predictive value of the probenecid test.** Journal of Nervous and Mental Disease. 158(5):331-337, 1974.

Preliminary results suggesting that the probenecid test is of predictive value regarding efficacy of treatment with 5-hydroxytryptamine (5-HT) precursors in depression are examined. Although the number of patients investigated was small, results suggest that 5-hyddroxytryptophan (5-HTP) benefits depressed patients showing a subnormal cerebrospinal fluid 5-hydroxyindoleacetic acid response to probenecid. The relevant implications of these data are that 1) 5-HT deficiency is etiopathogenic in some depression, b) the probenecid test can be of diagnostic value in such patients, and c) 5-HT precursors, specifically 5-HTP, may be an effective treatment modality in such individuals. 23 references. (Author abstract modified)

184653 Messiha, F. S.; Savage, C.; Turek, I.; Hanlon, T. E. Dept. of Psychiatry and Pharmacology and Therapeutics, Texas Tech Univ. School of Medicine, Lubbock, TX 79409 **A psychopharmacological study of catecholamines in affective disorders.** Journal of Nervous and Mental Disease. 158(5):338-347, 1974.

Relationships of treatment, symptom display, and catecholamine (CA) excretion are reported in the context of lithium carbonate and electroconvulsive therapy (ECT) administration in various types of psychiatric disorders. Data consists of mean effects on selected groups before and after treatment and of longitudinal case study material with each treatment modality. Group data reveals that 8 out of 10 manic patients display increased dopamine (DA) excretion at the height of their manic phases. Following stabilization with lithium, the excretion of urinary DA for the group returned to normal output. Regarding ECT, data for separate groups of 7 and 8 patients, respectively, reveals a tendency for DA and homovanillic (HVA) excretion to increase following ECT exposure. Results are discussed with reference to available information regarding the relationship of urinary DA excretion to mood and movement disorders. 59 references. (Author abstract modified)

184962 Deniker, P.; Ginestet, D.; Loo, H.; Zarifian, E.; Cottereau, M.-J. no address **/A preliminary study on the action of thyrotropine releasing hormone or TRH in depressive states./** Etude preliminaire de l'action de la thyreostimuline hypothalamique (thyroptropine releasing hormone ou T.R.H.) dans les etats depressifs. Annales Medico Psychologiques (Paris). 1(2):249-255, 1974.

A brief introduction to the use of thyrotropine releasing hormone (TRH) is given. Its effects on 18 patients suffering from mental depression are described. The results show some contradictions with regard to previous publications; only five cases showed any improvement. The analysis of the five cases show that in comparison to the success of tricyclic antidepressants and shock treatments, TRH is not to be considered an effective or certain medication. 10 references.

185007 Martin, Ian C. A.; Townend, R. A. Winterton Hospital, Sedgefield, Co. Durham, DL3 GHY England **Implications of sustained release phenothiazines: a study of fluphenazine decanoate.** British Journal of Psychiatry (London). 124:173-176, 1974.

The implications of sustained release phenothiazines are discussed, based on an 18 month study of fluphenazine decanoate. Subjects were 40 long-term psychotic patients, of whom 22 were male, mean 53 years old, and 17 female, mean 59 years old. Doses of decanoate ranged from 12.5mgm. every 6 weeks to 75mgm. weekly. One male was removed because of severe extrapyramidal symptoms. Findings indicate that, with one exception, all patients maintained a satisfactory clinical state, with a substantial tendency for some degree of improvement (41%). Side-effects were few (30% of cases), all extrapyramidal and, with the exception mentioned, all easily controlled by antiparkinson agents. A control study was deliberately not designed, because concern was not with evidence of improvement, but rather to demonstrate that existing clinical states could be more simply maintained with less time wasted on routine drug rounds. 14 references.

185747 Rickels, Karl; Weise, Charles C.; Csanalosi, Irma; Chung, Hack R.; Feldman, Harold S.; Rosenfeld, Howard; Whalen, Edward M. 203 Piersol Bldg., University Hospital, 3400 Spruce St., Philadelphia, PA 19104 **Clomipramine and amitriptyline in depressed outpatients: a controlled study.** Psychopharmacologia (Berlin). 34(4):361-376, 1974.

Clomipramine (75-125mg/day), a new tricyclic antidepressant, was compared to amitriptyline (75-125mg/day) in a double-blind six week trial carried out with 93 psychiatric and 75 nonpsychiatric depressed outpatients. Clomipramine tended to produce more side-effects, particularly of a sedative nature, was associated with greater dosage deviation and attrition, and appeared slightly faster in its onset of action than amitriptyline. While amitriptyline produced significantly more improvement than clomipramine according to several endpoint measures, a number of improvement criteria showed both agents to be of comparable efficacy. Clomipramine was most effective in the less depressed nonpsychiatric patients; amitriptyline was especially effective in the more depressed psychiatric patients. 18 references. (Author abstract modified)

185873 Noyes, Russell, Jr.; Dempsey, G. Michael; Blum, Aleksandar; Cavanaugh, Gary L. University of Iowa College of Medicine, 500 Newton Road, Iowa City, IA 52242 **Lithium treatment of depression.** Comprehensive Psychiatry. 15(3):187-193, 1974.

Previous findings on the utility of lithium treatment in unipolar and dipolar depressions are reexamined. Lithium carbonate in high doses was administered to 22 patients hospitalized for endogenous depression. A statistically significant difference in response was observed between bipolar and unipolar patients. All six with a prior history of mania responded to the drug, whereas only 44% of those without such a history showed a favorable response. Among the 13 patients that responded to lithium, a dose of 1800mg daily was well tolerated despite the development of mild neuromuscular side-effects in many. A clinical response that first appeared between the sixth and thirteenth days of lithium administration generally plateaued by the end of 3 weeks. Following placebo substitution, symptoms reemerged in nine patients. This investigation has again shown that bipolar depressions are more responsive to lithium than are unipolar ones. It suggests that further efforts be made to identify those unipolar depressions having a high probability of responding to lithium. 24 references. (Author abstract)

185928 Murphy, Dennis L.; Baker, Max; Goodwin, Frederick K.; Miller, Halbert; Kotin, Joel; Bunney, William E., Jr. Laboratory of Clinical Science, NIMH, Bethesda, MD **L-Tryptophan in affective disorders: indoleamine changes and differential clinical effects.** Psychopharmacologia (Berlin). 34(1):11-20, 1974.

The behavioral and metabolic effects of L-tryptophan in depressed and manic patients was examined. Large oral doses of L-tryptophan yielded negligible antidepressant effects in unipolar depressed patients but partial antidepressant and antimanic effect in some patients with bipolar affective disorder. Marked changes in cerebrospinal fluid, platelet and urinary levels of serotonin and 5-hydroxyindoleacetic acid in the patients during L-tryptophan administration suggest that the low response rate of severely depressed patients is probably not attributable to impaired L-tryptophan metabolism during depression. 53 references. (Author abstract modified)

186188 Prien, Robert F.; Caffey, Eugene M., Jr.; Klett, C. James. Central Neuropsychiatric Laboratory, VA Hospital, Perry Point, MD **Factors associated with lithium response in the prophylactic treatment of bipolar manic-depressive illness.** VA Research Report No. 96. Perry Point, MD, Veterans Administration, 1974. 14 p.

Possible predictors of lithium response are discussed in terms of a multihospital collaborative study evaluating prophylactic lithium therapy in 205 patients with bipolar manic - depressive illness. Factors associated with poor lithium response are: 1) a recent history of frequent affective episodes requiring hospitalization, and 2) previous failure on lithium. Results also suggest that lithium response may be related to the presence of schizo-affective illness and a family history of bipolar affective illness, but the small numbers of patients in these groups limit interpretation. Most lithium failures occur during the first year. Ability to remain on a maintenance lithium schedule with no episodes for a year may be the most potent predictor of ultimate success with lithium prophylaxis. The implications of these findings for the clinician selecting patients for prophylactic treatment are discussed. 22 references. (Author abstract modified)

186189 Prien, Robert, F. Central Neuropsychiatric Laboratory, VA Hospital, Perry Point, MD **The clinical effectiveness of lithium: comparisons with other drugs.** VA Research Report No. 97. Perry Point, MD, Veterans Administration, 1974. 19 p.

Studies comparing lithium with other drugs are examined. Lithium has been compared with chlorpromazine and methysergide in acute mania, imipramine and desipramine in acute depression, imipramine in recurrent mania and depression, chlorpromazine in schizo-affective and schizophrenic illness, and chlorpromazine, perphenazine, and thioridazine in other disorders. These comparisons suggest that lithium is more effective than chlorpromazine in the therapeutic treatment of mildly severe mania and is superior to imipramine in the prophylactic treatment of bipolar affective illness; otherwise, the comparative studies indicate no major advantage to using lithium in place of other treatments. However, it should be remembered that lithium has been compared with only a few drugs in generally small sample trials. It is concluded that lithium promises much to the field of pharmacotherapy, but requires more extensive evaluation to define its advantages and disadvantages with regard to other available treatments. 58 references. (Author abstract modified)

186190 Prien, Robert F. Central Neuropsychiatric Laboratory, VA Hospital, Perry Point, MD **Prophylactic treatment of recurrent depression: observations from a multihospital collaborative study.** VA Research Report No. 98. Perry Point, MD, Veterans Administration, 1974. 15 p.

Issues surrounding long-term maintenance chemotherapy in recurrent affective illness are discussed in terms of a recently completed multihospital study in which 116 patients with a history of recurrent endogenous depressions were treated over a 2 year period with imipramine, lithium carbonate, or placebo. Patients started treatment following discharge from hospitalization for acute depression. Treatment outcome was evaluated primarily in terms of occurrence of affective episodes: It is concluded that: 1) lithium and imipramine were significantly more effective than placebo in preventing both relapses and episodes; 2) the majority of patients who did not have episodes did have mood shifts which interfered in varying degrees with interpersonal and vocational adjustment; and 3) treatment outcome on lithium and imipramine was related to presence or absence of a history of manic episodes. Implications of these findings are discussed. 21 references. (Author abstract)

186191 Prien, Robert F.; Caffey, Eugene M., Jr. Central Neuropsychiatric Laboratory, VA Hospital, Perry Point, MD **Guidelines for antipsychotic drug use.** VA Research Report No. 95. Perry Point, MD, Veterans Administration, 1974. 15 p.

Rational utilization of antipsychotic drugs is discussed, as well as some of the common misuses of these drugs, including inadequate dosing, polypharmacy, multiple daily administration, prolonged use of antipsychotic drugs, and failure to periodically evaluate the patient's regimen. Alternatives to daily medication -- the drug holidays and long acting injectable drugs -- are also examined. Antidepressant and antianxiety agents are also considered although, in general, prescribing practices with these drugs have not been studied as adequately as with antipsychotic agents. 48 references. (Author abstract modified)

186580 Carlson, Harold E.; Robbins, Jacob; Murphy, Dennis L. NIH Clinical Center, 10-8N315, Bethesda, MD 20014 **The effect of lithium on thyroid iodine release in patients with primary affective disorder.** Psychopharmacologia (Berlin). 35(3):249-256, 1974.

Thyroid iodine release measured by the double isotope method of Nicoloff was studied in patients with manic-depressive illness before, during and after treatment with lithium carbonate. The urinary 125I/131I isotope ratio was measured following administration of Na125I-thyroxine. In three of four subjects, lithium caused a transient decrease in diurnal variation and a temporary reduction in the normal increase of the 125I/131I ratio during the first week of therapy or after a lithium dose increase. In addition, in two of three subjects, a rebound increase in the isotope ratio occurred following cessation of lithium administration. These changes most likely represent a direct inhibitory effect of lithium on the thyroid iodine release process. 17 references. (Author abstract)

186920 Gershon, Samuel; Shopsin, Baron. New York University School of Medicine, New York, NY **Lithium: its role in psychiatric research and treatment.** New York, Plenum Publishing, 1973, 358 p. $19.50.

Lithium's underlying modes of action in affective disorders are explored. A review of literature is included and the clinical effects of lithium as a psychoactive influencing behavior are examined. The cyclic and unipolar groups of manic-depressive disorders are discussed and a report on their natural clinical courses is presented.

187114 Meltzer, H. Y.; Crayton, J. W. Department of Psychiatry, University of Chicago Pritzker School of Medicine, Chicago, IL **Muscle abnormalities in psychotic patients: II. Serum CPK activity, fiber abnormalities, and branching and sprouting of subterminal nerves.** Biological Psychiatry. 8(2):191-208, 1974.

The serum creatine phosphokinase (CPK) activity, morphology of skeletal muscle fiber biopsies, and morphology of subterminal motor nerves of 24 psychotic patients of the common functional types and three of their first degree relatives were studied. Sixteen of the 24 patients had increased serum CPK activity, 17 of the 24 patients had muscle fiber abnormalities, and 16 of 24 had pathological changes in the morphology of the subterminal motor nerves. Five of the 24 patients had no abnormalities of any type. Similar abnormalities of msucle fibers and subterminal nerves were present in the relatives of the patients. The abnormalities of the subterminal nerves included branching, sprouting, axonal swelling, and degenerate nerve endings. The absolute and functional terminal innervation ratios (ATIR and FTIR, respectively) of the patients and relatives were significantly greater than those of the six controls without psychiatric illness. The increase in the ATIR and FTIR strongly suggests that the muscle fiber abnormalities in psychotic patients and their relatives are neurogenic in etiology. This is supported by the presence of fiber type grouping in several biopsies and the high correlations between the ATIRs and FTIRs and the number of scattered atrophic fiber in the entire group of muscle biopsies. 32 references. (Author abstract modified)

187115 Saletu, B.; Simeon, J.; Saletu, M.; Itil, T. M.; DaSilva, J. Department of Psychiatry, Missouri Institute of Psychiatry, School of Medicine, University of Missouri, St. Louis, MO **Behavioral and visual evoked potential investigations during trihexyphenidyl and thiothixene treatment in psychotic boys.** Biological Psychiatry. 8(2):177-189, 1974.

Behavioral and visual evoked potential (VEP) investigations were carried out in a group of hospitalized psychotic boys on placebo, during administration of an antiparkinsonian drug, trihexyphenidyl, as well as during concomitant thiothixene and trihexyphenidyl treatment. While there were no statistically significant clinical changes from placebo to trihexyphenidyl, a significant global and symptomatic improvement was observed as early as in the second week of thiothixene treatment. There were improvements in quantity and quality of motor activity, quantity and content of speech, social relationships with adults, anger, mood lability, emotional unresponsiveness, feeding difficulties, and attention disorders. Evaluation of VEPs demonstrated a significant latency decrease and a trend towards amplitude increase during trihexyphenidyl administration as compared with placebo, which suggests a stimulatory effect of this drug on the CNS. During thiothixene treatment a significant augmentation of both latency and amplitude occurred. Based on discriminant function analysis of VEP data of untreated psychotic children, psychotic children receiving thiothixene, and matched normal controls, it was concluded that the drug treatment resulted in a normalization of the evoked potential findings. 31 references. (Author abstract modified)

10 DRUG TRIALS IN NEUROSES

182428 Frommer, Eva A. Child Psychiatric Clinic, St. Thomas' Hospital, London S.E. 1, England **Indications for antidepressant treatment with special reference to depressed preschool children.** In: Annell, A., Depressive states in childhood and adolescence. Stockholm, Almqvist & Wiksell, 1972. 541 p. (p. 449-454).

At the Fourth Congress of the Union of European Pedopsychiatrists in Stockholm, August 30 - September 3, 1971, contrasting features of aggressive and nonaggressive depressed preschool children who were treated with antidepressants in a psychiatric clinic were discussed. Children in both groups had a high incidence of anorexia, enuresis, abdominal pain, insomnia, and maternal depression. Nonaggressive Ss were more often anxious, often had a precipitating stress, had more intact families, and came from better socioeconomic backgrounds. They made a group response to treatment and were usually suitable for simple outpatient therapy with antidepressants. Aggressive Ss had more disintegrated families and poor social backgrounds. They were more rejected by their parents and had more encopretic and enuretic problems, as well as antisocial behavior. They had a poor response to treatment and a higher rate of relapse. They probably require more vigorous environmental therapy than was offered to this sample. 11 references. (Author abstract modified)

182429 Kuhn, Verena; Kuhn, Roland. Kantonale Psychiatrische Klinik, CH-8596 Munsterlingen, Switzerland **Drug therapy for depression in children. Indications and methods.** In: Annell, A., Depressive states in childhood and adolescence. Stockholm, Almqvist & Wiksell, 1972. 541 p. (p. 455-459).

At the Fourth Congress of the Union of European Pedopsychiatrists in Stockholm, August 30 - September 3, 1971, the effectiveness of antidepressant drug therapy with a sample of depressed children was briefly discussed. The effectiveness or ineffectiveness of treatment is quite independent of the endogenetic or psychogenetic background. Drugs are given orally and consist of tricyclic antidepressants of the imipramine type. Although side-effects are common, they are not severe enough to require discontinuation of treatment. Good results have also been obtained with CIBA 34,276-Ba, and octadiene preparation with a ring structure different from that of imipramine. Only a few of the Ss could be considered to suffer from the classic type of melancholia, and the primary symptom is morning tiredness. Many of the symptoms can first be attributed to faulty upbringing or to neurotic tendencies, but these can be eliminated by careful examination. Drug therapy caused by disorders to disappear within a few days, despite the fact that no change took place in external environment or in the emotional makeup of the patient.

182432 Lelord, G.; Etienne, Th.; Veauvy, N. Centre Hospitalier Regional 'Bretonneau', 37-Tours, France /**Action of Opipramol (G 33.040) in depressive syndromes in children and adolescents.**/ Action de l'Opipramol (G 33.040) dans les syndromes depressifs de l'enfance et de l'adolescence. In: Annell, A., Depressive states in childhood and adolescence. Stockholm, Almqvist & Wiksell, 1972. 541 p. (p. 473-478).

At the Fourth Congress of the Union of European Pedopsychiatrists in Stockholm, August 30 - September 3, 1971, the effectiveness of Opipramol (G 33040) in treating childhood and adolescent depression was described, based on observations with 76 cases of such symptoms. In 54 cases there were remissions for several months to 4 years. The drug was very effective in reactive depression, in those with somatic manifestations, in those involving character changes, and in neurotic depression. It was not prescribed for malancholia, since it can only be given orally. However, its antidepressive effect on sadness, inhibition, and asthenia ap-

pears to be more marked than its sedative effect on anxiety and insomnia. The drug is well tolerated and may be considered a useful antidepressant in the outpatient treatment of children. Its chemical structure resembles most closely that of the antidepressent imipramine and the neuroleptic sedative, perphenazine. 8 references. (Author abstract modified)

182551 Sueta, Tazuko; Tanaka, Akemi. Department of Neuropsychiatry, Tokyo Women's Medical College, Tokyo, Japan **Clinical study of antidepressant agent, Noveril.** Journal of Tokyo Women's Medical College (Tokyo). 41(3):173-180, 1971.

A clinical study of the antidepressant agent 'Noveril' is presented. Forty eight patients with endogenous depression were treated with Noveril (Dibenzepin). The treatment produced the following results: good, 22%; better, 48%; no change, 22%, worse, 4%; and 4% became manic. Good and better results were obtained in the mild cases of simple depressive state, e.g.,the form of vital retardation with vital depressive mood. In addition to the effects on mood and retardation, a slight tranquilizing effect was also observed. None of the effects was as severe as those of Imipramine, Amitriptyline and Levomepromazine. Good and better results were obtained with a daily dosage of 240-480mg. Side-effects were few and slight. Among the side-effects were various types of sleep disturbance in almost half the cases. 11 references. (Author abstract modified)

182731 Kawano, Michio; Yoshimuta, Tadashi; Okubo, Naoyoshi; Takayama, Iwao. Faculty of Medicine, Kagoshima University, Japan **Clinical experience with a new psychotropic drug: FK-880 (sulpride), its effect on patients with psychosomatic diseases and psychoneurosis.** Journal of Japanese Psychosomatic Society (Tokyo). 13(3):188-195, 1973.

The effect of FK-880 on psychosomatic diseases and psychoneurosis was studied in 17 patients with neurosis, 3 patients with psychosomatic disease, and 6 patients with masked depression treated with FK-880 (150-300mg/day for 14-63 days, orally). The drug was effective in 80.8% of patients with neurosis and psychosomatic diseases, and 83.3% of patients with masked depression. This drug was significantly effective on depressive feeling, decrease of volition, sleep disturbance, anxiety, irritation, headache, fatigue, loss of appetite, dizziness, tachycardia, unpleasant feeling in the chest, and effective on hypochondriac symptoms and delusions of persecution. Side-effects, such as constipation, loss of muscle strength, and secretion of milk were observed among those treated with the drug in high doses. 13 references.

182764 Bonn, J. A. Academic Department of Psychological Medicine, St. Bartholomew's Hospital, London, E.C. 1, England **Some recent advances in the management of anxiety.** Postgraduate Medical Journal (Oxford). 48(Suppl. 4):24-26, 1972.

A comparison of oxypertine, diazepam and placebo in the management of neurotic anxiety was described in a symposium on the pharmacology and clinical use of oxypertine in anxiety held at Cambridge in 1972. Results of a double-blind, between patient comparison of oxypertine, diazepam and placebo in a patient mediated dose schedule for the management of neurotic anxiety are reported. Sixty patients suffering from neurotic anxiety, divided into three groups, received either 10mg oxypertine, 5mg diazepam or placebo. In self-assessment measures, the Morbid Anxiety Inventory demonstrated that with oxypertine, 17 of 19 improved; with diazepam, 13 of 20, and with placebo, 13 of 19. The bias of personally important life events favored the placebo group; after correcting for this, oxypertine showed significant superiority over placebo. Clinical ratings also showed oxypertine significantly superior to diazepam and placebo. The patient mediated dose schedule resulted in 28mg of oxypertine taken daily and 14mg diazepam. Pursuit rotor and reaction time measurements were taken in patients on full doses of the three treatments: placebo produced significantly less impairment than oxypertine and oxypertine produced less impairment than diazepam. Diazepam produced significantly more side-effects than placebo, but oxypertine did not. It is concluded that oxypertine is a useful drug in the management of anxiety, and of particular advantage in the ambulant patient. 4 references.

182766 Forrest, A. D.; Maule, M. Gogarburn Hospital and Royal Edinburgh Hospital, Edinburgh, Scotland **A controlled trial of oxypertine in patients with anxiety.** Postgraduate Medical Journal (Oxford). 48(Suppl. 4):30-32, 1972.

Oxypertine was compared with chlordiazepoxide in a controlled trial in 23 patients with anxiety in a paper presented before a symposium on the pharmacology and clinical use of oxypertine in anxiety held at Cambridge in 1972. Each patient received either 60 capsules of oxypertine (10mg) or chlordiazepoxide (15mg). Results demonstrated no difference between the groups. It was found that oxypertine was as effective over 4 weeks as chlordiazepoxide in the treatment of anxiety symptoms. No significant side-effects were reported in either group. Success was defined as reduction in total score on the Hamilton Anxiety Scale. There was no significant difference between the success and failure rates of the patients based on which drug was administered. This indicates that oxypertine is as effective as chlordiazepoxide in the treatment of anxiety symptoms and its use by family doctors is justified. 2 references.

182767 Salkind, M. R. St. Bartholomew's Hospital, London, E.C. 1, England **Anxiety neurosis in general practice.** Postgraduate Medical Journal (Oxford). 48(Suppl. 4):34-41, 1972.

A discussion of anxiety, with emphasis on the defense and coping mechanisms, the role of depression, the use of the Morbid Anxiety Inventory (MAI) and drug treatment was presented at a symposium on the pharmacology and clinical use of oxypertine in anxiety held at Cambridge in 1972. Anxiety is any apprehension of an event that is to take place; a neurotic anxiety state is the sum of multiple minor and major phobic states produced over the life span of the individual. Defense mechanisms used to prevent anxiety from reaching that state of conscious awareness, such as avoidance, denial, repression and regression, are discussed. Coping mechanisms, which function at a more superficial level, such as oral or touch satisfaction, laughing, crying and daydreams are reviewed. Most neurotic anxiety cases are short-term with multiple, mainly psychic, symptoms and with depression coexisting with anxiety. The MAI may be used to clarify anxiety shift states. A self-assessment inventory in multiple choice form is used to establish basal levels with individuals. Drug treatment for anxiety is important because of the association with depression; tricyclics with the addition of oxypertine are helpful. If depression is an important element, an anxiolytic combined with protriptyline or imipramine is recommended. The clinical effectiveness of oxypertine, its value in preserving alertness and its low risk of producing dependency in anxious patients assure it a place in the management of anxiety. 10 references.

182768 Murphy, J. E.; Margetts, G. Clinical Research Group, Northampton, England **Measurement of anxiety in general practice.** Postgraduate Medical Journal (Oxford). 48(Suppl. 4):41-43, 1972.

A simple, rapid anxiety rating scale that can be used by general practitioners to make a fairly accurate assessment of their patient's needs is discussed in a paper presented before a symposium on the pharamcology and clinical use of oxypertine in anxiety held at Cambridge in 1972. The Graphic Visual Anxiety Scale is compared with a modified Hamilton Anxiety Rating scale in which severity of symptoms was graded. Forty four patients (ages 21-65) suffering from anxiety states were assessed by both scales upon entry into the trial. After 2 weeks of Integrin (oxypertine), the two assessments were reported by the same doctor and results of the two methods of rating were compared. A high correlation between the two scores was observed in regard to the assessment of a patient's condition at a particular time and in recording changes in the condition. Only three patients showed no improvement; both scales showed that 90% of the patients improved following Integrin therapy. It is felt that the graphic scale is sufficiently accurate to enable a doctor to assess correctly the progress of a patient and only a small amount of time is required to produce a meaningful permanent record which can be compared with subsequent assessments. The disadvantage of this doctor rating scheme is that results of two different doctors on one patient cannot be directly compared. Patient rating scales may be used to overcome this failing.

182769 Mungavin, J. M. Medical Department, Winthrop Laboratories, Surbiton-upon-Thames, Surrey, England **A multicentre clinical trial of oxypertine in anxiety neurosis.** Postgraduate Medical Journal (Oxford). 48(Suppl. 4):47-50, 1972.

A multicenter study of 633 patients with anxiety neurosis measured by a modified Hamilton Rating Scale, using severe standards to assess the success of the treatment with oxypertine was reported at a symposium on the pharmacology and clinical use of oxypertine in anxiety held at Cambridge in 1972. There was an absolute success rate of 76%. The overall incidence of severe side-effects necessitating termination of treatment was 6%; 17% had mild side-effects, especially drowsiness, but continued treatment. Any undue sedation could be reduced by omitting the midday dose of oxypertine. A marked effect on depressed mood was observed in 75% of the patients who were noted to have depression on entering the trial. There was excellent patient acceptance of oxypertine and in 80% of patients oxypertine was rated the same or better than the previous medication. From these findings it was concluded that oxypertine (Integrin) is a most useful anxiolytic for treatment of patients in general practice. 3 references. (Author abstract modified)

182789 Montanini, R.; Gasco, P.; Manfredini, G. Divisione Neurologica Dell'Ospedale Generale Provinciale di Gallarate, Italia **/The use of low doses of monochlorimipramine in the therapy of neurotic depressive syndromes./** L'impiego della monoclorimipramina a bassi dosaggi nella terapia delle sindromi depressive neurotiche. Riv. Sper. di Freniatria e Med. Legale delle Alienazioni Ment. (Reggio). 97(1):147-164, 1973.

The use of low doses of monochlorimipramine in treating neurotic depressive syndromes is discussed. Good results were obtained in a preliminary study on 28 patients, confirming the marked antidepressant and anxiety reducing effect of the drug. A specific trial on 32 patients with nonendogenous depressions (anxious neurotic, reactive and hypochondriacal) is described. The adopted evaluation criteria were Hamilton scales for depression and anxiety, and overall assessment expressed by patients and investigators. After 4 weeks of therapy, anxiety symptoms were reduced by 76% and depression values by 72%. 35 references. (Journal abstract modified)

182829 Salelkar, G. K. no address **/Masked depression./** Depressio sine depressione. Clinician (Goa). 37(4):134-135, 1973.

The symptoms and treatment of 'masked depression', or 'depressio sine depressione', are examined in an editorial. In this disorder, physical symptoms are so pronounced that they overshadow the usual depressive manifestations -- thus diagnosis is difficult. The use of benzodiazepines and monoaminoxidase inhibitors in treatment of this neurotic depression is discussed and it is suggested that reassurance and psychotherapy are as important as drugs in many cases.

183362 Lapierre, Y. D.; Lavallee, J.; Tetreault, L. Hospital Pierre Janet, Hull, P.Q., Canada **Simultaneous mesoridazine and psychodrama in neurotics.** Intern. J. of Clinical Pharmacology, Therapy and Toxicology (Munchen). 7(1):62-66, 1973.

A double-blind factorial study of 24 outpatient neurotics of both sexes is reported as they underwent simultaneous drug (mesoridazine) and psychodrama treatment. Significant overall improvement was observed on the Wittenborn Psychiatric Rating Scale from the third to the sixth week of treatment for Ss on mesoridazine. The active drug associated with induced theme psychodrama treatment was accompanied by a decrease in obsessive-compulsive phobic symptomatology. No significant decrease in the neuroticism index of the Eysenck Personality Inventory was observed, but mesoridazine produced a significant decrease in the extroversion index in the first 3 weeks. This then rose to previous levels. There was a marked tendency for the Ss on mesoridazine to participate less actively in the psychodrama sessions. The quality of their participation showed significantly less affective involvement and their interventions, when present, were less involved and more neutral affectively. 4 references. (Author abstract)

183369 Ohtani, Tohru; Tatebe, Atsushi; Yamamoto, Norihito. National Maizuru Hospital, Maizuruu, Japan **So-called masked depression and its treatment.** Kyoto Igaku-kai Zasshi. 20(2):59-65, 1971.

Characteristics of masked depression and its treatment are discussed, based on 27 patients with anxiety neurosis, 14 with hypochondriasis, and 34 with minor depression. Most of the hypochondriac patients had depressive tendencies in their background, and most of the patients with minor depression had physical problems. The Tatabe-Guilford Test revealed that the patients with hypochondriasis and minor depression have similar personality profiles. The patients were treated with amitriptyline, with or without diazepam and nitrazepam, which induced remarkable improvement in 26% of the patients with anxiety neurosis, 50% of the patients with hypochondriasis and 57% of those with minor depression within 2 months. No significant side-effects were observed. 18 references.

183546 Kotin, Joel; Post, Robert M.; Goodwin, Frederick K. Orange County Medical Center, 101 City Drive S, Orange, CA 92668 **Delta9-Tetrahydrocannabinol in depressed patients.** Archives of General Psychiatry. 28(3):345-348, 1973.

The failure of delta9-tetrahydrocannabinol to produce euphoria or antidepressant responses in eight hospitalized depressed patients administered the drug in a double-blind study is evaluated. Four patients who received the drug for 7 days showed little change in mood but reported considerable drowsiness. In four patients, the drug trial was shortened because of adverse reactions; two of these patients experienced severe anxiety reactions with depersonalization after

a single dose. Effects on cognitive functioning and vital signs were similar to those reported by other investigators in normal subjects. It is emphasized that the results were obtained with a small sample of hospitalized inpatients with moderate to severe depression. Different effects might be observed in other settings or in patients with less severe symptoms. 17 references. (Author abstract modified)

183807 Beumont, P. J. V.; Carr, P. J.; Gelder, M. G. Department of Psychiatry, Groote Schuur Hospital, Observatory, Cape Town, South Africa **Plasma levels of luteinizing hormone and of immunoreactive oestrogens (oestradiol) in anorexia nervosa: response to clomiphene citrate.** Psychological Medicine (London). 3(4):495-501, 1973.

In a study of 11 patients with anorexia nervosa, plasma levels of luteinizing hormone (LH) and of estrogens (estradiol) were found to be low while the subjects were emaciated. After weight gain, hormone values rose and two patients spontaneously resumed menstruation. Clomiphene citrate was administered on one or more occasions to five patients, and bleeding was induced in the majority of those whose weight exceeded 80% of standard. In two of these patients an irregular cycle resumed for a brief period thereafter. Clomiphene appeared to be of limited practical value in the management of patients with anorexia nervosa, but the study provided some elucidation of the relationship between body weight and the menstrual disturbance in this condition. 15 references. (Author abstract)

184175 Rickels, Karl; Pereira-Ogan, Jorge A.; Case, George; Csanalosi, Irma; Mirman, Merrill J.; Nathanson, Juliet E.; Parish, Lawrence C. Department of Psychiatry, University of Pennsylvania, 203 Piersol Building, University Hospital, 3400 Spruce St., Philadelphia, PA 19104 **Chlormezanone in anxiety: a drug rediscovered?** American Journal of Psychiatry. 131(5):592-595, 1974.

The efficacy of chlormezanone, an infrequently prescribed minor tranquilizer, was tested in a 6 week double-blind trial involving 154 anxious outpatients. The results showed that chlormezanone (800 mg/day) was significantly more effective than placebo and was equal in effectiveness to chlordiazepoxide (50mg/day). Chlormezanone produced significantly more sedation and more side-effects, but no more attrition, than chlordiazepoxide. 7 references. (Author abstract)

184445 Malpas, Ann; Legg, N. J.; Scott, D. F. Dept. of Pharmacology and Therapeutics, London Hospital Medical College, London E1 1BB England **Effects of hypnotics on anxious patients.** Britist Journal of Psychiatry (London). 124:482-484, 1974.

The effects of hypnotics on anxious patients were examined. Hypnotics were given in courses lasting 7 days to patients in a double-blind placebo controlled study. Effects were assessed weekly on subjective, behavioral and EEG ratings. After a course of the drug, but not of placebo, the EEG shows impairment in terms of drowsiness and sleep. Anxious patients appear to have fewer persistent effects with hypnotics than the normals examined in an earlier investigation, a finding of considerable importance to psychiatric practice, and a starting point for future study on ambulant patients. 10 references. (Author abstract modified)

184845 Ito, Hitoshi. Department of Neuropsychiatry, Keio University, School of Medicine, Japan **Classification and indication of antianxiety agents in clinical practice.** Journal of Japanese Psychosomatic Society (Tokyo). 13(4): 235-240, 1973.

Various antianxiety drugs are described and classified. The chemical synthesis, dosage recommendation, indications and side-effects of these drugs are considered. 14 references.

185078 Sethna, E. R. All Saints' Hospital, Lodge Road, Birmingham, B18 5SD, England **A study of refractory cases of depressive illnesses and their response to combined antidepressant treatment.** British Journal of Psychiatry (London). 124:265-272, 1974.

Refractory cases of depressive illnesses and their response to combined antidepressant treatment were studied. Subjects were 12 patients at All Saints' Hospital, Birmingham, who were studied over a period of 2 years. Patients suffering from depressive illnesses which proved refractory to treatment by tricyclic antidepressants, monoamine oxidase inhibitors (MAOIs) and ECT were collected for a trial on a combination of phenelzine and amitriptyline. The patients who had proved refractory to treatment were all found to be suffering from neurotic depression with longstanding neurotic and personality disorders. Combined antidepressant therapy proved to be significantly more effective than the previous antidepressant treatment. Adverse reactions to combined antidepressants were no worse than to antidepressants used singly. Possible reasons for the adverse reactions reported in the literature are discussed, and ways of preventing them are suggested. 53 references. (Author abstract modified)

185210 Kellner, Robert; Collins, A. Cowan; Shulman, Robert S.; Pathak, Dorothy. Dept. of Psychiatry, School of Medicine, University of New Mexico, Albuquerque, NM **The short-term antianxiety effects of propranolol HCl.** Journal of Clinical Pharmacology. 14(5&6):301-304, 1974.

The short-term antianxiety effects of propranolol in anxious neurotic outpatients was assessed. Most Ss had anxiety neurosis and a few had depressive neurosis. Propranolol HCl was compared with matched placebo tablets in a double-blind crossover design. The median therapeutic dose was 112mg daily. In this dosage, propranolol HCl had neither marked short-term anxiolytic action no rapid sedative action. It is suggested that propranolol HCl may have useful effects in patients with somatic symptoms in which beta-adrenergic stimulation predominates. 13 references.

185322 Weissman, Myrna M.; Klerman, Gerald L.; Paykel, Eugene S.; Prusoff, Brigitte; Hanson, Barbara. Yale University School of Medicine, Dept. of Psychiatry, Depression Research Unit, 100 Park St., New Haven, CT 06511 **Treatment effects on the social adjustment of depressed patients.** Archives of General Psychiatry. 30(6):771-778, 1974.

The effects of maintenance treatment on social adjustment are examined in depressed outpatients randomly assigned to 8 months of amitriptyline hydrochloride, a placebo, or no pill, with or without psychotherapy, using a 2 x 3 factorial design. Results for the 106 patients who completed the trial show a significant main effect for psychotherapy, apparent only after 6-8 months' treatment. Psychotherapy improved overall adjustment, work performance, and communication, and reduced friction and anxious rumination. There was no effect on the patients' social adjustment for amitriptyline, and there were no drug psychotherapy interactions. Results support the value of weekly maintenance psychotherapy in recovering depressives. Since amitriptyline has been shown to reduce relapse and prevent symptom return, and psychotherapy was shown to enhance adjustment, there is evidence for combined treatments. 37 references. (Author abstract)

185874 Goldberg, Harold L.; Finnerty, Richard J.; Cole, Jonathan O. Dept. of Psychiatry, Boston University School of Medicine, Boston, MA **A study of anti-anxiety effects of WY-4036.** Comprehensive Psychiatry. 15(3):195-200, 1974.

The clinical action of the new benzodiazepine, WY-4036 (Lorazepam), was investigated in psychoneurotic patients, with the main target symptom anxiety. The analysis of differential response to a 4 week treatment of 60 patients with moderate or severe anxiety at intake treated with placebo and Lorazepam showed no significant drug effects at the end of 2 weeks. At the end of 4 weeks, a trend in favor of Lorazepam subjects on global severity of illness was found. The different rates of improvement between drug groups on the individual items showed Lorazepam to more significantly reduce several physical symptoms, while the Lorazepam subjects failed to achieve the same rate of improvement on cognitive or intellectual symptoms as placebo patients. The concern produced by these results is not that the active drug is a more effective agent in treating somatic symptoms of anxiety but rather that Lorazepam could be considered to be sufficiently disquieting to prevent improvement in cognitive and intellectual areas at the rate expected without an active psychopharmacological agent. There was a suggestion in the data that Lorazepam might be relatively more effective than placebo in patients with even more severe pretreatment anxiety symptoms than those included in the present study. 2 references. (Author abstract modified)

186584 Bianchi, G. N.; Fennessy, M. R.; Phillips, J.; Everitt, B. S. 238 Simpson's Rd., Bardon West, Queensland, Australia 4065 **Plasma level of diazepam as a therapeutic predictor in anxiety states.** Psychopharmacologia (Berlin). 35(2):113-122, 1974.

An oral test dose of diazepam was given to 25 anxious neurotics before they received 3 weeks of treatment with the drug. Blood was taken at 1 h and 2 h after the test dose (and during subsequent treatment) and the plasma levels of diazepam at these times were assayed. Ratings to assess subsequent clinical response were made in the context of a double-blind trial. The 2 h plasma level correlated positively with the steady state plasma level of diazepam after 1 week of treatment. There was a statistically strong link between a low 2 h plasma diazepam level and improvement after the first week of treatment. This correlation of low pretreatment plasma level with good response suggests either that there may be an avid uptake of diazepam from the blood in those who are going to improve clinically as a result of its administration, or that good responders have a special ability to form active metabolites of diazepam. A high 2 h plasma level was found in those patients who reported increased tiredness during the 3 weeks on diazepam. The 1 h plasma diazepam level, in contradistinction, had but negligible correlations with steady state levels, with clinical response and with diazepam induced tiredness. 13 references. (Author abstract)

186780 Penningroth, R. Paul; Steinmeyer, Charles H. Department of Psychiatry, University of Iowa College of Medicine, Iowa City, IA 52240 **Treatment of anxiety neurosis by alpha and beta adrenergic blocking agents.** Journal of the Iowa Medical Society. 64(5):205-207, 1974.

The salutary effects of propranolol upon anxiety symptoms are reviewed in a case study. Chemotherapy is provided for a severe anxiety neurotic, emphasizing both an alpha-adrenergic and beta-adrenergic blocker. Anxiety symptoms can result from any of several processes, only one of which is excessive beta-adrenergic excitation. The patient discussed experienced significant reductions in his anxiety level when taking high levels of both phenothiazine and propranolol. Thus, effective reduction of severe anxiety may be achieved by blockade of the specific endogenous transmitter at the postsynaptic receptors involved. 8 references. (Author abstract modified)

11 DRUG TRIALS IN MISCELLANEOUS DIAGNOSTIC GROUPS

182431 Polvan, Ozgur; Cebiroglu, Ridvan. Department of Child Psychiatry, Istanbul University, Istanbul, Turkey **Treatment with psychopharmacologic agents in childhood depressions.** In: Annell, A., Depressive states in childhood and adolescence. Stockholm, Almqvist & Wiksell, 1972. 541 p. (p. 467-472).

At the Fourth Congress of the Union of European Pedopsychiatrists in Stockholm, August 30 - September 3, 1971, the effectiveness of treating childhood depression with psychopharmacologic agents was discussed, based on observations of such treatment at a Turkish university clinic. Of 1248 children seen during 1970, 29 were diagnosed as depressed. These cases were considered in three subdiagnostic groups (classical, reactive, and neurotic depressive reactions) and a basic combination of drugs was chosen for each group, with other drugs directed to emotionally induced bodily symptoms being added where needed. Treatment lasted 8 weeks at the end of which each case was reevaluated by clinical and psychometric methods. The reactive depressives benefited most and classical depressives the least from the drug treatment, while neurotic depressives were in the middle. In classical and neurotic depression, in which there is a stronger depressive component, drug treatment should be supported with some form of psychotherapy. 7 references. (Author abstract modified)

182435 Tomas, Dostal. Psychiatric Research Institute, Praha 8-Bohnice, Czechoslovakia **Antiaggressive effect of lithium salts in mentally retarded adolescents.** In: Annell, A., Depressive states in childhood and adolescence. Stockholm, Almqvist & Wiksell, 1972. 541 p. (p. 491-498).

At the Fourth Congress of the Union of European Pedopsychiatrists in Stockholm, August 30 - September 3, 1971, 14 severely mentally retarded aggressive adolescents who received lithium treatment for 8 months in daily doses of 6-48mEq/patient, with serum lithium levels ranging from 0.30-0.95mEq/1, were described. Lithium seems to exert a sinigificant affect damping and antiaggressive effect in mentally retarded males previously resistant to phenothiazines. The most marked therapeutic effects were those achieved in cases with clinically documented alternating periods of more deteriorated behavioral disturbances and periods of relative calm and in such cases in which the affectivity inclined to lability. Excessive polydipsia connected with highly undisciplined fluid intake and polyuria associated with frequent bed wetting, however, represented a considerable limitation of the use of lithium in these states. 18 references. (Author abstract modified)

182550 Kawahara, Ryuzo. Department of Neuropsychiatry, Tottori University School of Medicine, Japan **An electroencephalographic study on the tolerance of the various psychiatric and neurological patients to the hypnotic effects of diphenhydramine -- measured by the amounts of sleep EEG as an indicator.** Journal of the Yonago Medical Association (Yonago). 23(1):73-91, 1972.

Tolerance to diphenhydramine (Dph) in normal and neuropsychiatric subjects was investigated. Results included: the percentage of waking electroencephalogram (EEG) periods in

69 normal Ss was 35.6plus or minus 29.0% on an average, with no differences in age and sex. The averages of the percentage of waking EEG periods after the Dph injection are listed for schizophrenics, manic-depressive patients, epileptics and patients with organic brain diseases. They were all significantly higher than the average of normal controls. The high tolerance to the effect of Dph was supposed to be due not only to the psychic state such as anxiety and tension of the S, but also to the constitution and other biological factors underlying the pathology of the diseases. The neurophysiological mechanism of the hypnotic effect of Dph as well as that of tolerance to it was discussed. 45 references. (Author abstract modified)

182595 Ferngren, H. G. Department of Pediatrics, Karolinska Sjukhuset, 10401 Stockholm 60, Sweden **Diazepam treatment for acute convulsions in children: a report of 41 patients, three with plasma levels.** Epilepsia (Amsterdam). 15(1):27-37, 1974.

Forty one children with prolonged convulsions were treated with diazepam. Seizures were arrested in 29 patients but recurred within 12 hours in 14. Respiratory arrest occurred in two patients after intravenous diazepam but not after intramuscular injection. Plasma levels of diazepam and N-desmethyldiazepam in three children showed that diazepam declines rapidly after intravenous injection; levels above 130ng/ml were necessary to keep one patient free of seizures. Three cases are presented to explain some of the limitations of diazepam therapy. 16 references. (Author abstract modified)

182624 Namba, Tsunehiko; Nishida, Kohei; Nozawa, Akira; Kato, Giichi; Saito, Toshiji; Tsutsui, Sueharu. School of Medicine, Toho University, Omori, Tokyo, Japan **Double-blind crossover comparison of bromazepam and diazepam in psychosomatic disease, neurosis and depression.** Journal of the Medical Society of Toho University (Tokyo). 20(3/4):445-456, 1973.

A double-blind test comparison of the effects of bromazepam (BZP) and diazepam (DZP) on various nervous disorders was conducted on 48 outpatients, consisting of 25 with psychosomatic disease, 11 having neurosis and 12 with depression. Three or four tablets of both drugs were administered using a crossover method for 2 weeks. There were no significant differences between bromazepam and diazepam in total, in each disease and in most of the syndromes. But BZP was significantly effective for sleep disturbances with the significance level more than 5%, DZP was significantly effective for anxiety, tension and fatigue. BZP was significantly effective for the feeling of head heaviness and also effective for stiff shoulder, sleep disturbances, anxiety and tension. Both drugs caused drowsiness and thirst rather frequently with no significant difference between the two. Results show that BZP can be used as a tranquilizer with some merits. 5 references. (Author abstract modified)

182790 Di Trapani, G.; Pinto, F. Clinica delle Malattie Nervose e Mentali, Universita Cattolica del Sacro Cuore di Roma, Rome **/Treatment of cerebrovascular disturbances with 2-Butylamino-1-(p-hydroxyphenyl) ethanol sulfate (Bamethan)./** L'1-(4 ossifenil)-1 ossi-n.2 butilaminoetano solfato (Bamethan) nelle insufficenze di circolo cerebrale. Riv. Sper. di Freniatria e Med. Legale delle Alienazioni Ment. (Reggio). 97(1):165-173, 1973.

Treatment of patients with cerebrovascular disturbances with Bamethan is reported. Treatment was concluded after 4 weeks and EEG controls were made. Of seven patients with acute cerebral disturbances two died from preexisting mitral cardiopathic and neurological causes and five received additional therapy; a slight deterioration of symptoms was noted. Eight patients with subacute or chronic disturbances showed good to very good results upon completion of treatment. Additional encephalographic data as well as detailed clinical observations are reported. 15 references.

182890 Estrada, Horacio R. U. P. - Philippine Center for the Health Sciences, College of Medicine, Philippines **Psychotropic drugs in childhood disturbances.** Philippine Journal of Pediatrics (Manila). 22(3):145-148, 1973.

The use of psychotropic drugs in childhood disturbances was explored. General comments on the use of drug effectiveness, use for childhood depression, use with psychotic children, classification, physiologic changes in children and dosage are included. The following drug types are discussed: the major tranquilizers; the minor tranquilizers; the antidepressants; the central nervous system stimulants; and hypnotics. 9 references.

182900 Sichel, J.-P.; Baldauf, A.; Fonlupt, V.; Poupier, G. Service de Psychiatric du Centre Hospitalier L.-Pasteur, 68 Colmar, France **/Experiments in oral and injectable forms of a new antidepressant (doxepine) on forty patients./** Experimentation de la forme orale et injectable d'un nouvel antidepresseur (doxepine) chez 40 malades. Annales Medico Psychologiques (Paris). 2(2):272-281, 1972.

Doxepine, a new tricyclic compound derived from dibenzoxepine, was evaluated for its antidepressive effect on different forms of depression in 40 patients. Twenty received the drug orally, the other 20 i.m. with occasional oral administration. The action of the doxepine on each symptom of depression is charted. It is concluded that doxepine does have antidepressant properties and associated sedative effects. Oral administration of the drug does not present any new elements when compared to other medications of the same type. The injected doxepine however, was found to be slightly less active than other injectable imipramines, much easier to handle, and less toxic. It is concluded that doxepine has a definite therapeutic value. (Author abstract modified)

182901 Martin, A.; Masson, J.-M.; Quentin, J.-C.; Verrier, J.-P. Travail du Service de Psychotherapie Femmes, C.H.U. Bretonneau, 37-Tours, France **/Benzoctamine in psychiatry: a 30-case study./** La benzoctamine en psychiatrie a propos de 30 cas. Annales Medico Psychologiques (Paris). 2(2):282-286, 1972.

The anxiolytic properties of benzoctamine are examined. A test was made on the effects of the drug in 30 women suffering from neuroses or psychoses. The average dose administered was 30mg. In the neurotic cases benzoctamine was generally the only medication administered; in the psychotic cases where the strain of anxiety was too tense neuroleptics were given in addition to the benzoctamine. Tolerance to the drug was excellent; no modification in the arterial pressure or in the blood was observed. In the neurotic states the anxiolytic effect of the drug was often associated with sleepiness during the day, this sleepiness was noted only during the beginning of the testing. In the psychotic states a higher dose of the drug (60mg) was necessary to relieve the anxiety, even then the delirium processes were not affected. It is concluded that benzoctamine is a choice anxiolytic agent, but that it does not have a favorable effect on agitation or personality problems.

183030 Jacques, Daniel. no address **/Study of the use of disulfiram implant in the treatment of alcoholism./** Etude de l'utilisation de l'implant de disulfirame dans le traitement de la

maladie alcoolique. Lausanne, Centre International d'Alcoologie/Toxicomanies, 1973. 37 p.

The effectiveness of subcutaneous implantation of disulfiram in treating alcoholism is discussed. This method of treatment aids in rehabilitating the patient socially and frees him from the constraints of taking daily oral medication. The physicochemical action of the implant is less powerful than that caused by injection of disulfiram in the bone, but its psychological effects are extremely important. It is necessary for the therapeutic program to deal with the any castration symbols and to avoid all suggestive action. The technique is simple; few problems have been encountered; and the risks are minimal. It cannot be used abruptly, because it must be preceded by a type of care classified as 'everyday therapy'. (Author abstract modified)

183124 Dachary, J. M. Centre Psychologique, 72700 Allones, France **/The use of Flupentixol in therapy./** Le Flupentixol en pratique hospitaliere. Information Psychiatrique (Lyon). 48(7):757-758, 1972.

A study on oral flupenthixol is reported. In borderline psychotic and schizophrenic states the drug was found to produce a disinhibitory effect with improved social contact, and a better adjustment to home life and profession. Its effect on character and behavioral problems was slight; no effect on hallucinatory psychoses was noted. It is concluded that flupenthixol is of undeniable interest for use in borderline cases. It may also be useful in certain depressive states where inhibition and lethargy do not respond well to antidepressants.

183191 Reyntjens, A. M. Janssen Pharmaceutica, B-2340 Beerse, Belgium **A series of multicentric pilot trials with pimozide in psychiatric practice: I. Pimozide in the treatment of personality disorders.** Acta Psychiatrica Belgica (Bruxelles). 72(6):653-661, 1972.

Assessment of the clinical efficacy and side-effect liability of pimozide in the treatment of patients exhibiting personality disorders is made. One hundred twenty patients were originally administered combinations of neuroleptics and other psychotropic agents and evaluated for drug efficacy and side-effects. The same 120 were then administered pimozide and evaluated as in the previous test. A marked improvement is noted on a 39 item rating scale, compiled from the major symptoms mentioned in the definitions of the DSM II. Results show a moderate to marked improvement in most patients of their familiar and social integration, and to a lesser extent of their professional performance; side-effects were infrequent. 10 references. (Author abstract modified)

183192 Reyntjens, A. M. Dept. of Clinical Research, Janssen Pharmaceutica, B-2340 Beerse, Belgium **A series of multicentric pilot trials with pimozide in psychiatric practice: II. Pimozide in the treatment of behavioural disorders in childhood and adolescence.** Acta Psychiatrica Belgica (Bruxelles). 72(6):662-670, 1972.

An investigation of the efficacy of pimozide in the treatment of behavioral disorders in childhood and adolescence is presented. Fifty five children were treated by 22 psychiatrists for a period of 2 months. A marked improvement in behavior is noted on a 24 item scale using the symptoms mentioned in the definitions of the DSM II. A global evaluation confirms this improvement in the majority of patients. Results show that behavior at home and at school, especially with teachers and classmates, improved in most of the patients. Side-effects were found to be minimal. 12 references. (Author abstract modified)

183193 Reyntjens, A. M. Janssen Pharmaceutica, B-2340, Beerse, Belgium **A series of multicentric pilot trials with pimozide in psychiatric practice: III. Pimozide in the treatment of stress-induced psychic and functional disorders.** Acta Psychiatrica Belgica (Bruxelles). 72(6):671-676, 1972.

An investigation of the efficacy of pimozide in the treatment of 62 patients with stress induced psychic and functional disorders is presented. Twenty one psychiatrists collaborated in a 4 week trial. Psychotropic agents were administered in the immediate pretrial period and an evaluation was made of their side-effects and efficiency. Pimozide replaced the psychotropic agents and was evaluated along the same lines. The Hamilton Anxiety Rating Scale was used to evaluate therapeutic results. A marked improvement is noted in the psychic items of the HAR Scale and social integration and professional performance improved in the majority of patients. Side-effects were minimal, and oversedation was found to be virtually absent. 4 references. (Author abstract modified)

183197 Deberdt, R. Poperingesteenweg 10 bis, B-8900 Ieper, Belgium **Psychic fatigability, its features and drug therapy.** Acta Psychiatrica Belgica (Bruxelles). 72(6):708-720, 1972.

Psychic fatigability, caused by social and/or psychological stress is discussed, as a common syndrome in modern society. Predominant symptoms of the psychic tiredness conditions are listed, including: intellectual disturbances, mood fluctuations, feelings of inadequacy at work, insulation and hypochondriacal preoccupation with health, tiredness, sleep disturbances and psychosomatic disorders. Minor tranquilizers are suggested as not being effective in alleviating this condition. Low dose pimozide is found to be quite effective in a small sample of patients suffering from psychic fatigability. The Hamilton anxiety rating scale is used to evaluate patient's progress under the drug. 5 references.

183198 Collard, Jackie. Boulevard de la Constitution, 66, B-4000, Liege, Belgium **/Control of insomnia with a new benzodiazepine: the flunitrazepam or Ro 5-4200 (first investigations of phase I and controlled investigations of phase II)./** Le controle de l'insomnie par une nouvelle benzodiazepine: le flunitrazepam ou Ro 5-4200 (investigations princeps de phase I et controlee de phase II). Acta Psychiatrica Belgica (Bruxelles). 72(6):721-735, 1972.

The effectiveness of flunitrazepam (Ro 5-4200) in control of insomnia as compared to diazepam and nitrazepam is discussed. An initial uncontrolled investigation of 56 cases shows: the anxiolytic power of Ro 5-4200 is inferior to that of diazepam and nitrazepam; in the control of insomnia by benzodiazepines, its efficiency and potency are without equal. Mean dosage in medium insomnia is found to be 5mg. A controlled investigation compares Ro 5-4200 (5mg) to nitrazepam or Mogadon (10mg) and a placebo (lactose). The superiority of flunitrazepam is statistically suggested and clinically demonstrated. Flunidazepam is suggested as an improvement in the control of insomnia. 14 references. (Author abstract modified)

183199 Ciccarelli, G.; Nose, F.; Zuanazzi, G. F. Ospedale Neuropsichiatrico provincale de Verona-Ponton, I-Verona, Italy **Fluspirilene, a long-acting injectable neuroleptic.** Acta Psychiatrica Belgica (Bruxelles). 72(6):736-747, 1972.

A detailed picture of the action of the compound, fluspirilene, is presented along with information concerning its long lasting effects. Fifty hospitalized patients with schizophrenic and other acute psychoses are administered fluspirilene for varying lengths of time and evaluated for im-

provements in mental state by means of Sterkmans' questionnaire. Results show that fluspirilene's effects are comparable with those of other stronger neuroleptics. The margin between the neuroleptic effect and the parkinsonian effect is characteristic of this drug. It is suggested that this long effect places it among the best pharmocodynamic agents available. It is shown that fluspirilene is of great use for the treatment of hospitalized mental patients and those who refuse all medications. 19 references. (Author abstract modified)

183201 Aflalo, M.; Berkowitch, S.; Thielemans, G.; Vermeylen, J. Rue d'Aumale 21, B-1070 Brussels, Belgium **/Clinical assay of lorazepam with ambulant patients./** Experimentation clinique du lorazepam (Temesta) en pratique ambulatoire. Acta Psychiatrica Belgica (Bruxelles). 72(6):756-766, 1972.

A study of the anxiolytic and/or sedative effects of lorazepam carried out with a group of 50 ambulant psychiatric patients is discussed. The group was divided into 17 psychotics and 33 neurotics. Lorazepam was administered during a 2 month period with daily doses varying between 3 and 7.5mg. The effects of lorazepam were assessed by clinical pictures and by the Hamilton Anxiety scale. Results show that a constant dimunition of anxiety is manifested throughout the first week of the treatment. Sedative effects encountered at the beginning of the treatment were mitigated over time, but it seemed advisable to increase the dosage over a long period of time. The association of neuroleptic or thymoanaleptic drugs with lorazepam leaves intact its anxiolytic properties. (Author abstract modified)

184174 Waizer, Jonas; Hoffman, Stanley P.; Polizos, Polizoes; Engelhardt, David M. Department of Psychiatry, State University of New York Downstate Medical Center, 450 Clarkson Ave., Brooklyn, NY 11203 **Outpatient treatment of hyperactive school children with imipramine.** American Journal of Psychiatry. 131(5):587-591, 1974.

Nineteen hyperactive schoolchildren were treated in an outpatient clinic with imipramine for 8 weeks, followed by 4 weeks of placebo. On the basis of ratings by a child psychiatrist, parents, and teachers, significant improvement was observed in hyperactivity as well as in defiance, inattentiveness, and sociability. Placebo treatment resulted in deterioration of behavior. The side-effects of anorexia and insomnia were reported but represented no serious problem. The unique effects of imipramine and its advantages over central nervous system stimulants in the treatment of hyperactive children are discussed. 14 references. (Author abstract)

184177 Czerwinski, Anthony W.; Clark, Mervin L.; Serafetinides, Eustace A.; Perrier, Celia; Huber, Wolfgang. Department of Medicine, University of Oklahoma Health Sciences Center, Oklahoma City, OK **Safety and efficacy of zinc sulfate in geriatric patients.** Clinical Pharmacology and Therapeutics. 15(4):436-441, 1974.

The safety and efficacy of zinc sulfate were examined in geriatric patients (mean ages 73 and 77 years old). Using a double-blind design, 30 geriatric patients with the diagnosis of senile dementia were treated with zinc sulfate, 220mg three times daily, or with an identical appearing placebo for 24 weeks. Diarrhea occurred in six of 16 zinc treated patients and in one of 14 placebo patients. In zinc treated patients, plasma zinc concentrations increased during the first 4 weeks and thereafter stabilized at approximately 150 micrograms/dl. Psychometric and behavioral evaluations did not demonstrate a statistically significant difference between placebo and zinc treated patients. Some behavioral tests did indicate that zinc treated subjects deteriorated less rapidly than concurrent placebo subjects. 15 references. (Author abstract)

184195 Birdsong, Jackson H.; McKinney, Alexander S. Department of Physical Medicine, Woodruff Medical Center, Emory University, Woodruff Memorial Building, Atlanta, GA 30322 **Long-range motor performance changes in levodopa-treated patients with Parkinson's disease.** Neurology. 24(2):107-115, 1974.

A precise measurement of motor function, Methods - Time Measurement, was used to analyze motor performance in patients with Parkinson's disease receiving levodopa therapy. The data indicate an initial improvement, in all motions of the upper extremity, that reaches a maximum and then slowly declines over a period of years. Data indicated that Parkinson's disease continues to advance despite treatment with L-dopa. It is suggested that it is unlikely that a biochemical disorder is the basis of the illness. A basic neuropathologic disorder is concluded as responsible for inducing dopamine deficiency, so that arresting the condition will depend on identification and correction of this more fundamental defect. 12 references. (Author abstract)

184196 Miller, Edith. Division of Neurology, Maimonides Medical Center, 4802 10th Ave., Brooklyn, NY 11219 **Deanol in the treatment of levodopa-induced dyskinesias.** Neurology. 24(2):116-119, 1974.

The effectiveness of deanol in the treatment of levodopa induced dyskinesias in patients with Parkinson's disease was examined. Of 11 such patients treated with deanol in a single-blind controlled study, dyskinesias were completely eliminated in eight patients and were greatly improved in a ninth. One patient did not respond to the treatment. The remaining patient discontinued the medication after 2 days because of a feeling of fatigue. Otherwise no side-effects were noted and no laboratory abnormalities were encountered. Improvement began 10 to 14 days after initiation of treatment. In five patients treated successfully with deanol, placebo was substituted after 4 weeks, and dyskinesias reappeared within 3-8 days. 21 references. (Author abstract)

184964 Ostaptzeff, G.; Ostaptzeff, M.; Lavoine, J. R. no address **/Autocriticism and real place of the same medication (Vesprin)./** Autocritique et place reelle du meme medicament. Annales Medico Psychologiques (Paris). 1(2):264-277, 1974.

The use of triflupromazine hydrochloride (Vesprin) in conjunction with therapy in profoundly mentally debilitated children and adolescents is evaluated through results on the I.M.P.,I.M.Pro.,and the C.A.T. Indications for application of Vesprin are described. The good and bad aspects of the drug are noted, placing primary importance in the type of treatment methodology.

185008 Young, John; Hall, Peter; Blakemore, Colin. St. George's Hospital, Stafford, England **Treatment of the cerebral manifestations of arteriosclerosis with cyclandelate.** British Journal of Psychiatry (London). 124:177-180, 1974.

Treatment of the cerebral manifestations of arteriosclerosis with cyclandelate is discussed. Twenty one patients suffering from cerebral arteriosclerosis diagnosed on defined clinical criteria were treated with cyclandelate (1,600mg/day) in a double-blind, controlled cross over trial lasting 12 months. Patients were assessed on various psychiatric neurological, behavioral, psychometric and other parameters and deteriorated to a

statistically significant extent while having placebo treatment. This decline was absent in the cyclandelate treatment phase. 14 references. (Author abstract)

185190 Whyte, C. R.; O'Brien, P. M. J. Lynfield Mount Hospital, Bradford 9, Yorkshire, England **Disulfiram implant: a controlled trial.** British Journal of Psychiatry (London). 124: 42-44, 1974.

Results of treatment of 22 male alcoholics supplemented by disulfiram implantation are reported. Implantation was followed by a period of sobriety of 5.4months, which was significantly longer than that achieved by the same patients on previous occasions and by the control group. 6 references. (Author abstract)

185192 Singer, K.; Cheng, R.; Schou, M. University of Hong Kong, Queen Mary Hospital, Hong Kong **A controlled evaluation of lithium in the premenstrual tension syndrome.** British Journal of Psychiatry (London). 124:50-51, 1974.

The use of lithium in the premenstrual syndrome was investigated in a double-blind experiment involving 19 Chinese outpatients. Patients were selected on the basis of symptoms being temporally related to the menstrual period, including marked emotional tension and various somatic features. Results indicate that overall, patients made good improvement with lithium and with placebo; they did slightly better with lithium, but the differences were not significant. Some adverse reactions were noted. Results are compared with the literature; it is concluded that the main difference between the present study and others which indicated good results with lithium is the employment of placebo control periods. It is noted that the premenstrual tension syndrome is easily influenced by new treatments and other psychological factors. 2 references.

185193 Naylor, Graham J.; Donald, J. M.; Le Poidevin, David; Reid, Andrew H. Dept. of Psychiatry, The University of Dundee, DD1 4HN, Angus, Great Britain **A double-blind trial of long-term lithium therapy in mental defectives.** British Journal of Psychiatry (London). 124:52-57, 1974.

A 2 year double-blind trial of the prophylactic effect of lithium therapy was carried out on an inpatient group of mentally defective patients suffering from frequently recurring affective or behavioral changes. Fourteen patients completed the trial. The number of weeks ill during the year on lithium was significantly less than the number of weeks ill during the year on placebo. There appeared to be less effect on the actual number of episodes of illness. The number of episodes during the year on lithium was less than that during the year on placebo, but the difference was not statistically significant. 16 references. (Author abstract)

185875 Angrist, B.; Urcuyo, L.; Gershon, S. Neuropsychopharmacology Research Unit, New York University Medical Center, New York, NY **Response to incremental doses of Ditran in abstinent alcoholics and drug users.** Comprehensive Psychiatry. 15(3):201-204, 1974.

The hypothesis of differential sensitivity to anticholinergics in a mixed patient group of alcoholics and drug users was tested. The results fail to demonstrate an increased sensitivity to anticholinergics in alcoholics with past alcohol withdrawal psychoses. This does not mean that cholinergic mechanisms do not play a role in these psychoses. A more direct test would be a trial of efficacy of centrally active cholinesterase inhibitors, such as physostigmine or THA, in the treatment of these states. The possibility that alcoholism per se might lead to increased sensitivity to anticholinergics is suggested by these findings. This does not imply that a direct metabolic effect of alcohol is responsible. Rather, this finding might reflect increased vulnerability on the basis of subclinical organicity caused indirectly by alcoholism via deficiency states, frequent head trauma, or other factors. 6 references. (Author abstract modified)

185929 Gerlach, J.; Reisby, N.; Randrup, A. Stc. Hans Hospital, Dept. E, DK-4000 Roskilde, Denmark **Dopaminergic hypersensitivity and cholinergic hypofunction in the pathophysiology of tardive dyskinesia.** Psychopharmacologia (Berlin). 34(1):21-35, 1974.

The counterbalancing dopaminergic - cholinergic system was studied in a clinical pharmacological investigation of neuroleptic induced tardive dyskinesia. Eight hospitalized Ss aged 20 to 69 years were treated with alpha-methyl-para-tyrosine (AMPT), L-Dopa, physostigmine, scopolamine and biperiden. Results showed that AMPT significantly reduced, while L-Dopa and biperdin significantly precipitated/aggravated the dyskinesia. The effects of physostigmine and scopolamine have varied, which is discussed in relation to the existence of both hypocholinergic and hypercholinergic stereotype. It is concluded that dopaminergic hypersensitivity, cholinergic hypofunction and a reduced biological buffer capacity comprise important elements in the pathophysiology of tardive dyskinesia. Simple prophylactic and therapeutic directions are included. 44 references. (Author abstract modified)

186029 Chase, Thomas N.; Woods, Anne C.; Glaubiger, George A. Neurology Unit, NIH Clinical Center, 9000 Rockville Pike, Bethesda, MD 20014 **Parkinson disease treated with a suspected dopamine receptor agonist.** Archives of Neurology. 30(5):383-386, 1974.

A single-blind crossover trial of a putative dopamine receptor stimulating agent, piribedil, was conducted in 16 patients with idiopathic parkinsonism. At maximum dose levels overall improvement in parkinsonian signs averaged 30%. Adverse effects included gastrointestinal disturbances, behavioral alterations, and dyskinesias, but were severe enough to require drug withdrawal in only one patient. The antiparkinsonian efficacy of levodopa together with a peripheral decarboxylase inhibitor, tested in 12 of these patients, was about twice that of piribedil. Levodopa treatment failures due to toxic effects other than dyskinesias responded well to piribedil. As expected of a dopamine receptor agonist, piribedil substantially reduced the central turnover of this monoamine as estimated by the probenecid loading test. 20 references. (Author abstract)

186553 Khorana, Anand Bhushan. Department of Psychiatry, Medical College and S.S.G. Hospital, Baroda, India **A controlled trial of imipramine hydrochloride on enuresis.** Current Medical Practice (Bombay). 16(7):305-308, 1972.

A controlled trial of imipramine hydrochloride on enuresis is reported. Subjects were 100 children in good physical health and typical of patients usually diagnosed as having primary or essential enuresis. The age range was 5 to 15 years, with a mean age of 8.2years. Twenty six of the subjects were girls. Subjects were divided into two matched groups, A and B, of fifty patients each. During the first period of 12 weeks, Group A patients received imipramine and Group B patients placebo; during the second 12 week period, treatment was crossed over, Group A patients receiving placebo and Group B patients receiving imipramine. Results clearly establish the effectiveness of imipramine in enuresis. 17 references. (Author abstract modified)

186574 Monti, Jaime M.; Trenchi, Hugo M.; Morales, Francisco; Monti, Luis. Departamento de Farmacologia y Terapeutica, Hospital de Clinicas, Montevideo, Uruguay **Flunitrazepam (Ro 5-4200) and sleep cycle in insomniac patients.** Psychopharmacologia (Berlin). 35(4):371-379, 1974.

The action of flunitrazepam (Ro 5-4200), a benzodiazepine derivative, was assessed on the sleep cycle of insomniac patients by means of all night recordings. Baseline placebo nights were compared with the drug and with the placebo postdrug nights. Flunitrazepam induced a shift to faster frequencies of the electroencephalogram and a disappearance of sleep stages 3 and 4 while stage 2 was increased. In 10 out of 12 studied insomniacs the compound was effective in inducing and maintaining sleep (decrease in nonrapid eye movement (NREM) sleep latency, wake time and number of wakes) throughout the drug administration period. Both NREM and REM sleep were increased, the latter most likely in relation to blockade of processes precluding NREM emergence. The hypnotic action of flunitrazepam was still present during the first withdrawal night, pointing out to a carry over effect. 10 references. (Author abstract)

187236 Reintoft, Mogens. Geriatric Department, Albanigade 23, DK 5000, Odense, Denmark **Polymyalgia rheumatica in a geriatric department: nine patients with an average age of 83 years.** Gerontologia Clinica (Basel). 15(4):247-252, 1973.

Twelve patients with polymyalgia rheumatica (p.r.), or suspected of suffering from p.r.,registered in a geriatric department of 130 beds during a period of 33 months were studied. Nine of the patients (group I) with an average age of 83 years old, were found to fulfill the criteria laid down for the diagnosis, while the remaining three patients (group II) must be presumed to have suffered from some other diseases. The patients in group I were treated with steroids, which had an excellent effect on the symptoms and laboratory findings. At the time of followup, these patients had been treated on average for 14 months. It is concluded that the occurrence of p.r. in a geriatric department is similar to that reported from medical departments and that it is very important to be aware of this diagnosis in old people, as therapy is very effective. 7 references. (Author abstract)

12 PSYCHOTOMIMETIC EVALUATION STUDIES

184021 Beahrs, John O.; Carlin, Albert S.; Shehorn, Janice. University of Washington School of Medicine, Seattle, WA **Impact of psychoactive drugs on hypnotizability.** American Journal of Clinical Hypnosis. 16(4):267-269, 1974.

In a study of the impact of psychoactive drugs on hypnotizability, 11 adult male marihuana smokers were pretested for hypnotic susceptibility and retested under four experimental conditions: 1) after smoking a cannabis cigarette containing 7.5mg of tetrahydrocannabinol and receiving an intramuscular (IM) placebo injection; 2) after smoking a placebo cannabis cigarette and receiving an IM injection of 2mg of haloperidol; 3) after a combination of both drugs; and 4) after placebo smoke and placebo injection. The drugs had no systematic impact on hypnotizability as measured by a modified version of the Harvard Group Scale of Hypnotizability. 9 references. (Author abstract modified)

185083 Fernandez, J.; Brennan, T.; Masterson, J.; Power, M. St. Brendan's Hospital, Dublin, 7, Ireland **Cytogenetic studies in the offspring of LSD users.** British Journal of Psychiatry (London). 124:296-298, 1974.

A cytogenetic study on the offspring of LSD users is presented. Subjects were two apparently normal full-term male infants whose mothers had received known amounts of pure LSD as part of their psychotherapeutic management before they became pregnant. A profile of each mother is provided, and the dosages are recorded. Both male parents were healthy individuals with no history of drug abuse. Data failed to show evidence of chromosomal damage or congenital defect in the offspring. Hecht et al.,have emphasized that an improved understanding of possible remote and immediate teratogenic effects of LSD would depend on the reporting of children, both with and without malformations, born to parents who had been exposed to this substance. It is suggested that careful records be kept of all children born to LSD exposed parents. It is felt that burden of proof concerning the alleged mutagenic and teratogenic effects of d-LSD 25 in humans remains with the proponents of these assertions. 14 references.

186024 Martin, W. R.; Sloan, Jewell W. National Institute on Drug Abuse, Addiction Research Center, Lexington, KY **The possible role of tryptamine in brain function and its relationship to the actions of LSD-like hallucinogens.** Mount Sinai Journal of Medicine. 41(2):276-282, 1974.

The possible role of tryptamine in brain function and its relationship to the actions of LSD like hallucinogens are discussed. Data from several studies support the hypothesis that LSD and related hallucinogens exert many of their effects by serving as agonists of a tryptamine receptor. Data in man suggest that tryptamine could play a role in the pathologic functioning of the brain, for the infusion of relatively large quantities of tryptamine produces changes similar to those produced by LSD, including perceptual distortions. It is concluded that tryptamine may play a role in the normally functioning brain, and when present in excessively high quantities, may be responsible for pathologic functioning. 22 references.

186025 Leuner, Hanscarl. Psychiatrische Klinik der Universitat Gottingen, Von-Siebold-Strasse 5, D-3400, Gottingen, Germany /**Creativity and the state of consciousness.**/ Kreativitat und 'Bewusstseinsveranderung'. Confinia Psychiatrica (Basel). 16(3-4):141-158, 1973.

Use of hypnagogic, meditative or psychotoxic means of changing the state of consciousness to promote creativity is discussed. It was found that in certain phases of the creative process, stimulation through artificial alteration of consciousness is possible. The phenomena of regression make it possible to draw upon the vast reservoir of the unconscious. Suggestions for further research are included. 37 references. (Author abstract modified)

186026 Bader, A. Avenue de la Gare 2, CH-1003 Lausanne, Switzerland /**Hallucinogenic drugs and artistic creativity.**/ Halluzinogene Drogen und kunstlerische Kreativitat. Confinia Psychiatrica (Basel). 16(3-4):159-176, 1973.

A discussion between two painters, a sociologist with a particular interest in art, a doctor who owns an art gallery and four psychiatrists, during a working session of the German Language Society of Psychopathology of Expression, at Freudenstadt, in the Black Forest, September 23-24, 1972 is reported. The effects of the drugs on artistic creativity were evaluated, and various factors which might have an effect in such experiments were identified. It was recognized that a drug cannot itself have any creative virtue, but may induce a modification in style or stimulate the presentation of new raw material. Distinction between ordinary creativity and the more highly specialized creativity of the artist is drawn. The latter

entails a formal elaboration which permits communication to others, a function which is disturbed by the dru . Personal rug. conditions, the set, and environmental conditions are of fundamental importance. In the absence of adequate preparation, the artist is in danger of using up all his energy in combatting the intrusion into his familiar imaginary world of new phenomena produced by the drug. Such experiments raise many complex problems which are discussed in detail. The tests must be carried out without preconceptions and in a nonemotional atmosphere. It is felt that such research is promising, allowing exploration of phenomena which touch directly upon the mystery of human creation. 16 references. (Author abstract modified)

13 MECHANISM OF ACTION: PHYSIOLOGICAL, BIOCHEMICAL AND PHARMACOLOGICAL

182556 Sawada, Hideo; Hara, Akira; Yano, Hiroko; Kido, Akira. Department of Legal Medicine, Gifu University School of Medicine, Gifu, Japan **Blood level and urinary excretion of bromazepam in man.** ACTA Scholae Medicinalis Universitatis in Gifu (Gifu). 21(4):248-259, 1973.

Blood level and urinary excretion of bromazepam (BZ) in man were investigated. Both in male and in female patients except one female case, a correlation was recognized between the BZ blood level in the early period (2-4 hours) and the drug efficacy. In normal Ss, the interrelation was recognized only in a male patient. The excretion ratio in urine of BZ and its metabolites was found to be 50% and 20-30% in male and female patients respectively 72 hours after the administration of 20mg. In the normal cases, 70-80% was excreted in urine 72 hours after the administration of 5mg. The main metabolites in both patients and normals were 3-OH 2-amino-5-bromobenzoylpyridine (3-OH ABBP), followed by 3-OH BZ and ABBP. 5 references. (Author abstract modified)

182719 Hill, Shirley Y.; Schwin, Robert; Goodwin, Donald W.; Powell, Barbara J. Renard Hospital, 4940 Audubon Avenue, St. Louis, MO 63110 **Marihuana and pain.** Journal of Pharmacology and Experimental Therapeutics. 188(2):415-418, 1974.

Pain thresholds and tolerance, before and after smoking marihuana, were studied under a 'permissive' set of instructions for report of pain. Pain was created by cutaneous electrical stimulation applied to the subjects' fingers. It was found that marihuana affected thresholds by increased sensitivity to both painful and nonpainful stimulation and reducing tolerance for pain. 18 references. (Author abstract modified)

182722 Dinovo, Eugene C.; Gottschalk, Louis A.; Noble, Ernest P.; Biener, Robert. Neurochemistry Lab., Dept. of Psychiatry and Human Behavior, College of Medicine, Univ. of Calif., Irvine, CA 92664 **Isolation of a possible new metabolite of thioridazine and mesoridazine from human plasma.** Research Communications in Chemical Pathology and Pharmacology. 7(3):489-496, 1974.

The metabolism of thioridazine and mesoridazine was studied in humans by both gas chromatography (GC) and thin layer chromatographic (TLC) techniques, which indicate that a major unknown component which may be a metabolite of the two drugs is present in the plasma in all subjects tested. The component behaves toward mesoridazine as mesoridazine behaves toward thioridazine, suggesting that it is a metabolite of these two drugs. The new component was shown by GC and TLC not to be one of the six known metabolites of thioridazine. 6 references. (Author abstract modified)

183142 Chikvaidze, V. N.; Iordanishvili, G. S.; Sobchinskaya, N. M. no address **/The influence of neurotropic drugs on monoamine oxidase (MAO) and 5-oxytryptophane decarboxylase (5-OTD) activity in the brain./** Vliyaniye neyrotropnykh veshchestv na aktivnost' monoaminoksidazy i 5-oksitriptofandekarboksilazy v tkani mozga. Soobshcheniya Akademii Nauk Gruzinskoy SSR (Tbilisi). 70(1):201-203, 1973.

Chlorpromazine, melipramine, nardyl, reserpine, haloperidol, and ipraside were found to decrease the activity of monoamine oxidase in both chronic and acute experiments involving the brain. Amysil proved to be indifferent. Chlorpromazine, amysil, melipramine, and nardyl decreased, whereas reserpine increased the activity of 5-oxytryptophane decarboxylase. Haloperidol had no effect. 8 references. (Journal abstract)

183360 Ban, Th. A.; Lehmann, H. E.; Klingner, A. Division of Psychopharmacology, Department of Psychiatry, McGill University, Montreal, Quebec, Canada **Nicotinic acid and catechol-O-methyl-transferase activity in schizophrenia.** Intern. J. of Clinical Pharmacology, Therapy and Toxicology (Munchen). 7(1):44-47, 1973.

The hypotheses that prior and simultaneous administration of nicotinic acid to schizophrenic patients can prevent the exacerbation of psychopathology, which is induced by the combined administration of monoamine oxidase inhibitor and a methyldonor, and that nicotinic acid can attenuate or improve the psychopathology thus induced, were tested. Nicotinic acid could neither prevent nor counteract the clinical worsening due to methionine administration. In some instances, indications that nicotinic acid may have negative therapeutic effects were noted. Since aggravation of psychopathology was seen only in 70% of the methionine treated patients, it was speculated that aggravation of psychopathology to methionine is restricted to those schizophrenics with a high catechol-O-methyl-transferase activity. 17 references. (Author abstract)

183402 McQuillan, Loretta M.; Lopec, Carmencita A.; Vibal, Job R. 70-25 Yellowstone Blvd., Forest Hills, NY 11375 **Evaluation of EEG and clinical changes associated with pavabid therapy in chronic brain syndrome.** Current Therapeutic Research. 16(1):49-58, 1974.

Results of a double-blind study conducted over a period of 27 months indicate that changes in the predominant electroencephalographic (EEG) frequencies have definite application in the objective evaluation of changes associated with chronic brain syndrome. Analysis of Mental Function Test scores and predominant EEG frequencies after 2 months of treatment revealed an 80% improvement rate in the Pavabid (papaverine hydrochloride) treatment group vs a 2% improvement rate in the placebo treatment group. After 24 months, the EEGs of Pavabid patients still indicated improved or undeteriorated conditions, (50% improved, 50% unchanged), whereas 33% of the placebo group were improved and 66% had deteriorated. No adverse effects were encountered during the study and no evidence of drug related changes were reflected in extensive laboratory tests performed before, during and at the conclusion of the study. 8 references. (Author abstract)

183490 Evans, J. I.; Glass, D.; Daly J. R.; McLean, A. W. Sleep Laboratory, Department of Psychiatry, University of Edinburgh, Edinburgh, Scotland **The effect of Zn-tetracosactrin on growth hormone release during sleep.** Journal of Clinical Endocrinology and Metabolism. 36(1):36-41, 1973.

Serum growth hormone (GH) and plasma corticosteroid levels were measured in six healthy male subjects during sleep on several nights. Blood samples were taken through an indwelling catheter and sleep stage was monitored by continuous electroencephalograms (EEG). Zn-tetracosactrin given on the morning prior to a test night produced a sustained rise on plasma corticosteroid throughout the night, and eliminated the peak of GH release observed during early slow wave sleep on control nights. The EEG pattern of sleep was unaltered. 30 references. (Author abstract modified)

183603 Nagy, Adam; Treiber, Laszlo. Department II, Lillhagen's Mental Hospital, S-442 03 Hisings Backa, Sweden **Quantitative determination of imipramine and desipramine in human blood plasma by direct densitometry of thin-layer chromatograms.** Journal of Pharmacy and Pharmacology (London). 25(8):599-603, 1973.

Imipramine and desipramine were estimated in the plasma of patients receiving therapeutic doses of imipramine. The compounds were extracted as bases into n-heptane, separated by thin-layer chromatography and transferred into colored spots by an oxidative procedure. The quantification was made with a new densitometric technique of high sensitivity. The coefficient of variation was 11-16% at concentrations of 20 micrograms liter-1 (71.2nmol and 75.0nmol liter-1 for imipramine and desipramine respectively) and the recovery was 70-81%. 6 references. (Author abstract)

183604 Christiansen, Johs; Gram, Lars F. Department of Clinical Chemistry A, Righospitalet, Copenhagen, Denmark **Imipramine and its metabolites in human brain.** Journal of Pharmacy and Pharmacology (London). 25(8):604-608, 1973.

A quantitative and qualitative thin layer chromatographic study of the distribution of imipramine and its metabolites in 13 different regions of the brain in a fatal case of intoxication is reported. A quantitative thin layer chromatographic method for in situ determination of imipramine and desipramine has been developed. Eight identified and eight unidentified metabolites were detected in the different parts of the brain. Among the identified were hydroxy-, N-oxide, and iminodibenzyl-metabolites. The metabolic pattern found corresponds closely to the pattern found in human heart tissue and in urine from patients given imipramine. 11 references. (Author abstract modified)

183793 Grove, J.; Toseland, P. A.; Draffan, G. H.; Clare, R. A.; Williams, Faith M. Poison's Unit, Guy's Hospital, London, S.E. 1, England **Butobarbitone metabolism in man: identification of 3'-ketobutobarbitone.** Journal of Pharmacy and Pharmacology (London). 26(3):175-178, 1974.

In a study of butobarbitone metabolism in man, after single 200mg oral doses of butobarbitone (I), 5.4% was excreted in urine unchanged and 28.2% as the 3'-hydroxy metabolite (II) in 6 days. A new metabolite, the ketone (III), was detected in urine following oral administration both of I and of II. Oxidation of the hydroxy to the ketone metabolite was demonstrated in vitro with the 900g fraction of rat liver. Use was made of selective ion monitoring gas chromatography - mass spectrometry methods in metabolite detection. 10 references. (Author abstract)

183796 Beckett, A. H.; Belanger, P. M. Department of Pharmacy, Chelsea College, University of London, Manresa Road, London SW3 6LX, England **Metabolism of chlorphentermine and phentermine in man to yield hydroxylamino, C-nitroso- and nitro-compounds.** Journal of Pharmacy and Pharmacology (London). 26(3):205-206, 1974.

The metabolism of chlorphentermine and phentermine in man was examined. After an oral dose of chlorphentermine, 65mg, analysis of human urine gave peaks corresponding to the C-nitroso, nitro, and hydroxylamino compounds. About 10% of the dose of the chlorphentermine was obtained from urine as N-oxidation products. Less than 5% of phentermine (25mg) was obtained from the urine as N-oxidation products. 11 references.

184314 Tanaka, Masatoshi; Hirai, Tomoko; Inanaga, Kazutoyo; Isozaki, Hiroshi. Institute of Brain Diseases, Kurime University School of Medicine, Japan **The effect of flurazepam on the photopalpebral reflex.** Clinical Psychiatry (Tokyo). 16(2):193-202, 1974.

Hypnotic action of flurazepam (F) and nitrazepam (N) was studied in an experiment on 11 healthy college boys treated with F (15-30mg), N (5-10mg) or placebo with microvibration (MV) and photopalpebral reflex (PPR) examined for 240 minutes after drug treatment. F gradually increased the peak latency which reached a maximum of 2-3msec 180 minutes after F treatment and began to decrease 240 minutes after F treatment. N induced no significant change in the peak latency up to 90 minutes after N treatment, and gradually increased the peak latency thereafter, which reached a maximum of 4 msec 240 minutes after N treatment. This indicates that F has quicker hypnotic action but lasts for shorter time than does N. No significant change in MV was induced by F and N treatment. Those treated with F felt less drowsiness, weakness and dizziness than those treated with N. 13 references.

184437 Beumont, P. J. V.; Corker, C. S.; Friesen, H. G.; Kolakowska, T.; Mandelbrote, B. M.; Marshall, J.; Murray, M. A. F.; Wiles, D. H. Dept. of Psychiatry, Univ. of Cape Town, South Africa **The effects of phenothiazines on endocrine function: II. effects in men and post-menopausal women.** British Journal of Psychiatry (London). 124:420-430, 1974.

The effects of phenothiazines on endocrine function in men and postmenopausal women were studied. Plasma luteinizing hormone (LH), gonadal hormones and prolactin were investigated during chronic neuroleptic treatment and following drug withdrawal in 12 schizophrenic patients. In male subjects plasma testosterone during treatment was low or normal and rose on withdrawal of drugs, but there were no attendant changes in LH levels. In postmenopausal women plasma LH and estrogens were within the normal range and were not affected by changes in treatment. Plasma prolactin during treatment was elevated in female patients and within the normal range for males. Following drug withdrawal prolactin levels decreased in both male and female subjects. The response of growth hormone (GH) and cortisol to induced hyperglycemia and hypoglycemia was normal in all 13 patients tested during neuroleptic treatment. The group included eight patients with galactorrhea and/or elevated plasma prolactin. Increased plasma prolactin and suppressed plasma testosterone imply the possibility of selective neuroleptic effects on the hypothalamus level and on the peripheral gland respectively. 40 references. (Author abstract modified)

184654 Fann, William E.; Davis, John M.; Janowsky, David S.; Kaufmann, John S.; Cavanaugh, John H.; Oates, John A. Duke Univ. Medical Center and VA Hospital, Durham, NC 27710 **Effect of antidepressant and antimanic drugs on amine uptake in man.** Journal of Nervous and Mental Disease. 158(5):361-368, 1974.

The effect of antidepressant and antimanic drugs inprindole and lithium on amine uptake in man is examined. It is found

that iprindole, a clinically effective antidepressant drug, does not inhibit the amine uptake pump in rat brain or in human vascular tissue measured indirectly through norepinephrine (NE) or tyramine pressure studies. The disassociation of the antidepressant activities of inprindole from its inhibition of the amine pump casts doubt on the current monoamine hypothesis of depression. Lithium reduces the NE pressor response in man without significantly altering tyramine sensitivity. The therapeutic activity of lithium resides in several effects, such as increased amine uptake, decreased amine release, and decreased receptor sensitivity. 32 references. (Author abstract modified)

184978 Kanto, J.; Iisalo, E.; Lehtinen, V.; Salminen, J. Dept. of Pharmacology, University of Turku, 20520 Turku 52, Finland **The concentrations of diazepam and its metabolites in the plasma after an acute and chronic administration.** Psychopharmacologia (Berlin). 36(2):123-131, 1974.

The plasma diazepam, N-demethyldiazepam, and free oxazepam concentrations were studied in 12 neurotic outpatients during subchronic use, in 14 outpatients after chronic use, and in 8 test subjects after an acute intravenous administration. There are several reasons for believing that diazepam may induce its own metabolism in man: 1) the decrease in diazepam and N-demethyldiazepam concentrations in the plasma after 1-6 weeks therapy; 2) comparatively low plasma diazepam concentrations in patients who had taken diazepam for several months or years; 3) much higher concentrations of N-demethyldiazepam, the main metabolite, after intravenously given diazepam in chronic users of diazepam as compared to controls; and the decrease in the ability to form N-demethyldiazepam after abstinence, when diazepam was administered intravenously to a chronic user of diazepam before and after the abstinence of the drug. Diazepam should be administered in small doses and for short periods of time only, or intermittently. 15 references. (Author abstract modified)

185932 Kopell, Bert S.; Wittner, William K.; Lunde, Donald T.; Wolcott, Leslie J.; Tinklenberg, Jared R. Psychophysiology Laboratory, Dept. of Psychiatry, Stanford Univ. School of Medicine, Palo Alto, CA 94305 **The effects of methamphetamine and secobarbital on the contingent negative variation amplitude.** Psychopharmacologia (Berlin). 34(1):55-62, 1974.

The amplitude of the contingent negative variation (CNV) was studied in 12 male Ss given oral doses of methamphetamine, secobarbital and placebo on three testing days separated by one week. Orders were balanced across Ss and testing conditions were double-blind. The mean amplitudes of the CNV elicited with methamphetamine were significantly greater than those obtained with secobarbital and placebo. Comparing secobarbital with placebo yielded no significant results possibly due to the low secobarbital dosage. The sensitivity of the CNV amplitude to methamphetamine suggests that CNV may be a sensitive measure of arousal and attention and could provide a reliable index for assessing the relative arousal effects of complex drugs on humans. 27 references. (Author abstract)

185998 Messiha, Fathy S.; Morgan, John P. Dept. of Psychiatry, Texas Tech University School of Medicine, Lubbock, TX 79409 **Imipramine-mediated effects on levodopa metabolism in man.** Biochemical Pharmacology (Oxford). 23(10):1503-1507, 1974.

The effect of imipramine (IMP) on levodopa (L-dopa) metabolism was studied in four normal subjects. IMP pretreatment for 3 consecutive days prior to the administration of 500 mg L-dopa moderately decreased the urinary excretion of dopa. Similarly, IMP pretreatment decreased the urinary excretion of dopamine, norepinephrine and their major acid metabolites. In contrast, IMP pretreatment decreased the urinary excretion of serotonin but increased the excretion of its major acid metabolite, 5-hydroxyindoleacetic acid. Findings suggest that IMP mediated decreased excretion of dopa and its metabolites studied is partially related to retarded gastrointestinal absorption of L-dopa and that IMP may alter the metabolic pathway of serotonin during L-dopa administration in man. (Author abstract)

186184 Dasberg, Haim H.; van der Kleijn, Eppo; Guelen, Pieter J. R., van Praag, Herman M. Department of Biological Psychiatry, Psychiatric Clinic, University of Groningen, The Netherlands **Plasma concentrations of diazepam and of its metabolite N-desmethyldiazepam in relation to anxiolytic effect.** Clinical Pharmacology and Therapeutics. 15(5):473-483, 1974.

The relationship between clinical improvement, plasma concentrations and clearance rates in anxious patients undergoing oral psychotropic drug treatments was explored. Fifteen nonpsychotic patients suffering from acute anxiety in a crisis situation were treated orally with diazepam for 5 consecutive days as inpatients. Measurements were made on three levels while a control group of 15 similar patients received placebo. The design was double-blind and randomized. Results suggest that the degree of diazepam effect is directly proportional to plasma concentrations and reciprocal clearance values of diazepam and N-desmethyldiazepam. Monitoring of diazepam treatment on the basis of plasma concentrations is suggested. Implications for future research into the variability of response to drugs are discussed. 33 references. (Journal abstract modified)

186187 Molnar, George W.; Read, Raymond C. Veterans Administration Hospital, Little Rock, AR **Propranolol enhancement of hypoglycemic sweating.** Clinical Pharmacology and Therapeutics. 15(5):490-496, 1974.

The extent of sweating enhanced by propranolol was documented. Nineteen ulcer patients undergoing the Hollander test were selected as subjects. Oral propranolol doubled sweating during insulin induced hypoglycemia. Two of the seven hypoglycemic patients studied with propranolol alone did not sweat, establishing that propranolol does not initiate sweating either by discharges from the hypothalamus or direct action on sweat glands. Therefore, propranolol enhances hypoglycemic sweating either by blocking a beta-adrenergic agent (perhaps epinephrine) that inhibits secretion and potentiating the discharge of impulses by glocupenic neurons of the hypothalamus or possibly by competitive displacement of membrane calcium. The seasonal factor and frequency of administration of dosage of this experiment is also discussed. 23 references. (Journal abstract modified)

186745 Flemenbaum, Abraham. Dept. of Psychiatry, Texas Tech University School of Medicine, Lubbock, TX 79409 **Does lithium block the effects of amphetamine? A report of three cases.** American Journal of Psychiatry. 131(7):820-821, 1974.

Three case reports are presented supporting the hypothesis that lithium therapy inhibits the effect of amphetamine. It is suggested that the pharmacologic mechanisms of action of lithium and amphetamine are directly opposite and that lithium could be prophylactic for cases of amphetamine abuse. Further research to evaluate this hypothesis is suggested. 11 references. (Journal abstract)

187116 Ellinwood, Everett H., Jr.; Sudilovsky, Abraham; Nelson, Linda M. Department of Psychiatry, Duke University Medical Center, Durham, NC **Behavior and EEG analysis of chronic amphetamine effect.** Biological Psychiatry. 8(2):169-176, 1974.

Behavior and electroencephalographic (EEG) analysis of chronic amphetamine effect were studied. The limbic spindle was demonstrated to be sensitive both to the state of abnormal arousal and to changes leading to the bizarre behavioral manifestations in the chronic amphetamine intoxication paradigm. The high voltage, high frequency spindle was associated with epileptiform like discharges in the rhinencephalon which are, in turn, associated with the bizarre behavior. 23 references. (Author abstract)

187149 Vogel, William; Broverman, Donald M.; Klaiber, Edward L.; Kobayashi, Yutaka. Department of Psychology, Worcester State Hospital, Worcester, MA 01613 **EEG driving responses as a function of monoamine oxidase.** Electroencephalography and Clinical Neurophysiology (Amsterdam). 36(2):205-207, 1974.

Electroencephalogram (EEG) driving responses were studied as a function of monoamine oxidase. EEG driving responses to photic stimulation were significantly reduced in 10 normal young males following administration of isocarboxazid (Marplan), a monoamine oxidase inhibitor. Prior to drug administration, EEG driving responses were positively related to plasma monoamine oxidase activity levels. These results are interpreted as reflecting the effect of central adrenergic processes upon EEG driving responses to photic stimulation. 17 references. (Author abstract)

14 MECHANISM OF ACTION: BEHAVIORAL

182591 Bojanovsky, J.; Tolle, R. Universitats-Nervenklinik, D-44 Munster, Germany **/Influence of antidepressive therapy on the disturbed time estimation of depressives./** Der Einfluss der antidepressiven Therapie auf das gestorte Zeiterleben depressiver Patienten. Psychiatria Clinica (Basel). 6(6):321-329, 1973.

The time estimation of 31 depressive patients was tested in two ways: the patients had to estimate the length of a preceding discussion and then to estimate the length of the proceeding 2 1/2 minutes. The examinations were made before the start of the therapy, after therapeutic sleep deprivation and in the course of a 4 weeks amitriptyline therapy. Before treatment, the just passed discussion time was overestimated and the length of the 2 1/2 minutes was underestimated. After sleep deprivation, errors were still greater, although the condition of the endogenous depressions improved. With the amitriptyline therapy the changes were opposite to those of sleep deprivation. Results are discussed in relation to some previous experimental examinations and to the phenomenological analysis of the time sense of depressives. 17 references. (Author abstract)

182741 Freedman, Alfred M. New York Medical College, New York, NY **Clinical pharmacology of cannabis.** Final Report, NIMH Grant MH-18172, 1972, 75 p.

The effects of high and low dose marihuana, high and low dose delta9-tetrahydrocannabinol (THC) and high dose hashish on the central nervous system, mood, and behavior were studied in medical students. Marihuana and THC resulted in increased alpha activity in the EEG, hashish did not. All preparations elicited a decrease in beta activity and an increase in heartrate. These responses were dose related. All preparations resulted in increased subjective self-ratings of high. Short-term memory and reaction time were both adversely affected by high dose marihuana; these behaviors were not examined after administration of THC or hashish. Preliminary studies of the chronic administration of marihuana indicated that it is safe to administer daily for 21 days and suggest the possibility of tolerance in some behaviors. 27 references. (Author abstract)

182763 Ashton, Heather; Hall, Elizabeth H.; Savage, R. D.; Telford, Rosemary; Thompson, J. W. Department of Pharmacology, University of Newcastle upon Tyne, Newcastle upon Tyne, England **A small controlled study to determine the time of onset of action of oxypertine after oral administration in normal subjects.** Postgraduate Medical Journal (Oxford). 48(Suppl. 4):14-18, 1972.

The time of onset of action of oxypertine following a single oral dose of 20mg investigated in six male subjects using a double-blind controlled trial design and in two male subjects who knew they had received the drug was discussed in a symposium on the pharmacology and clinical use of oxypertine in anxiety held at Cambridge in 1972. A series of physiological (heartrate, blood flow and pressure) and behavioral (performance of mental arithmetic) measurements were made at regular intervals both before and after each subject received the drug. The usual increase in heartrate associated with a period of mental arithmetic was reduced or abolished by the drug. Blood pressure changes were negligible. Limb blood flow increased later, and could have been due to indirect causes, such as hunger. Performance on the pursuit rotor showed a decrement as the drug took effect and changes in mood occurred. It was concluded that the action of the drug on changes of heartrate produced by the stress of mental arithmetic, on performance on pursuit rotor and on mood began about 40 minutes after the ingestion of a single dose of 20mg. 2 references. (Author abstract modified)

183418 Narayanan, H. S.; Reddy, G. N. Narayana; Rao, B. S. Sridhara. All India Institute of Mental Health, Bangalore-27, India **A case of Kleine-Levine Syndrome.** Indian Journal of Psychiatry (Madurai). 14(3):356-358, 1972.

A case of Kleine-Levine Syndrome is reported, the second reported from India. The patient was a single male, 21 years old. His complaints were drowsiness, episodic attacks of excessive sleep, drinking of large quantities of water, tiresomeness, restlessness and irritability. His early developmental milestones were normal. At the age of 17 he was reported to have had a severe attack of typhoid from which he recovered in 3 months. Two years later he had a second attack. Following this he suffered from jaundice. Six months later he started showing episodic attacks of excessive sleep each lasting for 3 to 4 days. On the advice of their family physicians his parents took him to a psychiatrist who diagnosed his illness as acute psychosis. Shock therapy, chlorpromazine, trifluoperazine and imipramine all proved ineffective in controlling his symptoms. Within 2 weeks of initiation of methylamphetamine therapy the patient was alert and cooperative and remained so through a followup examination. 6 references.

183615 Avis, Harry H. Department of Psychiatry, University of California, San Francisco, CA 94122 **The neuropharmacology of aggression: a critical review.** Psychological Bulletin. 81(1):47-63, 1974.

The literature on aggression is reviewed from a multidisciplinary neuropharmacological standpoint. An examination of the literature revealed evidence for differentiating several kinds of

aggression. This differentiation could be seen in the psychopharmacological literature, where some compounds were effective in altering some forms of aggressive behaviors but ineffective in altering others. Differences in endogenous levels of neurotransmitters were also reported, but there was little correlation between changes in neurotransmitter systems and effectiveness of compounds supposedly altering these systems. A tentative hypothesis is offered which attempts to explain the behavioral effects of these drugs in terms of their action on several neurotransmitter systems. 132 references. (Author abstract)

184082 Greenwood, Monica H.; Lader, Malcolm H. Department of Psychiatry, Institute of Psychiatry, DeCrespigny Park, London S.E.5, England **A controlled comparison of the psychotropic effects of propanidid and methohexitone.** Behaviour Research and Therapy (Oxford). 12(1):19-27, 1974.

In a controlled comparison, six volunteer subjects were given infusions of the psychotrophic drugs methohexitone, propanidid, and saline. Propanidid caused less impairment of physical and psychological function than methohexitone. It is suggested that propanidid might serve as an alternative to methohexitone for inducing relaxation during systematic desensitization. 33 references. (Author abstract modified)

184291 Adler, R.; Gervasi, A.; Holzer, B. Department of Medicine, University of Berne, Berne, Switzerland **Perceptual style and pain tolerance -- II. the influence of an anxiolytic agent.** Journal of Psychosomatic Research (Oxford). 17(5-6):381-387, 1973.

To eliminate the psychological factor of anxiety in a study of the relationship between perceptual style and pain tolerance, an anxiolytic agent, Tacitin, was given to 41 male volunteers. A positive correlation between field orientation and pain tolerance was found in less anxious subjects, and Tacitin enhanced the correlation. However, interviews suggest that Tacitin did not exert its influence via a reduction of anxiety. It is suggested that Tacitin enhanced the correlation between field orientation and pain tolerance by reducing the activity in the motivational system and its contribution to the analysis of the afferent sensory system. 8 references. (Author Journal abstract modified)

184438 Perkins, Richard; Hinton, John. Academic Dept. of Psychiatry, Middlesex Hospital Medical School, London, W.1 England **Sedative or tranquillizer? A comparison of the hypnotic effects of chlordiazepoxide and amylobarbitone sodium.** British Journal of Psychiatry (London). 124:435-439, 1974.

The hypnotic effects of chlordiazepoxide and amylobarbitone sodium were compared. In a double-blind trial, which included a placebo, the EEG effects and subjective ratings of sleep were measured in psychiatric patients with insomnia; the subjects acted as their own controls. It was found that both drugs are hypnotics, but sodium amylobarbitone has a significantly greater effect than chlordiazepoxide when compared at the doses found equivalent for relieving anxiety. The hypnotic effect of chlordiazepoxide is not clearly related to dosage. The barbiturate decreases REM sleep, as expected, but chlordiazepoxide does not. The difference in actions of these two drugs is discussed briefly in terms of the site of action and the relief of insomnia by alleviating anxiety. 9 references. (Author abstract modified)

184618 Doenicke, A.; Feist, H. W.; Kugler, J. Anasthesieabteilung der chirurg. Poliklinik der Universitat Munchen, 8 Munchen 2, Pettenkoferstr. 8a, Germany **/Comparison of psychoexperimental performance under the influence of the analgesic propiramfumarate./** Psychoexperimentelle Leistungsvergleiche unter dem Einfluss des Analgetikums Propiramfumarat. Arzneimittel-Forschung(Aulendorf). 24(4a):693-696, 1974.

Psychoexperimental performance under the influence of the analgesic propiramfumarate is examined. The influence of N-(1-methyl-2-piperidino-ethyl)-N-(2-pyridyl)-propionamide-fumarate (propiramfumarate, Bay 4503) on human efficiency was investigated by psychoexperimental tests. In a double-blind study, 50 mg of propiramfumarate was compared with 50 mg of 10-(2-dimethylamino)propyl)phenothiazine, hydrochloride (promethazine, Atosil) and placebo after the participants' original behavior is first recorded. The psychoexperimental tests show that promethazine causes a decline in efficiency, which is significant in long-term efficiency tests. In some tests, however, propiramfumarate in comparison to placebo causes an increase in efficiency. Results show that propiramfumarate in comparison to placebo does not significantly deteriorate efficiency. 10 references. (Journal abstract modified)

184848 Linnoila, M.; Maki, M. Dept. of Pharmacology, Siltavuorenpenger 10, Helsinki 17, SF-00170, Finland **Acute effects of alcohol, diazepam, thioridazine, flupenthixole and atropine on psychomotor performance profiles.** Arzneimittel-Forschung (Aulendorf). 24(4):565-569, 1974.

Acute effects of alcohol, diazepam, thioridazine, flupenthixole, and atropine on psychomotor performance profiles were studied. An attempt was made to analyze by statistical means the effects of drugs on total performance rather than on single psychomotor variables. Subjects were 220 volunteer students in the age class of 20 years who were examined double-blind. Placebo was often experienced as an active drug, and some of the pyschomotor variables after placebo treatment were associated similiarly to those measure after diazepam. The active agents often impaired the ability to compensate impaired performance by slow driving and slow reactions. After thioridazine or diazepam some of the subjects tended not to compensate the impairment of skills by careful performance. Neither atropine nor flupenthixole showed any major interaction with alcohol, but the slight interaction observed between atropine and alcohol might take place on the central level. Flupenthixole proved deleterious for attention and information processing. 19 references. (Author abstract modified)

184963 Ostaptzeff, G.; Ostaptzeff, M.; Lavoine, J. R. no address **/The analysis of the potential action of a medication./** Analyse du champ d'action d'un medicament. Annales Medico Psychologiques (Paris). 1(2):255-264, 1974.

The therapeutic action of triflupromazine hydrochloride (Vesprin) is analyzed in 35 adults and 23 children between 8 and 69 years old. The results are viewed from a diagnostic and symptomatic aspect. Good results are shown in the treatment of aggressiveness, personality and behavioral disorders, and anxiety. It is concluded that Vesprin should be used for its sedative effect. The broad sample group may negatively affect the reliability of the results.

184976 de L. Horne, David J. University of Melbourne, Royal Melbourne Hospital, Victoria, 3050, Australia **L-Dopa effects on motor and 'central programming' deficits in Parkinsonism.** Psychopharmacologia (Berlin). 36(2):175-180, 1974.

The effects of treatment by L-Dopa on both motor and 'central programming' deficits in Parkinsonism were in-

vestigated. Nine patients with Parkinsonism were tested on psychomotor tasks involving both unimanual and bimanual performance, before and after treatment. Control data was obtained from 28 age matched Ss. These were only tested on one occasion. As expected, there was a very significant improvement in motor performance of the Parkinsonism group after treatment by L-Dopa. The evidence of improvement in the 'central programming' deficit was less conclusive, but seemed substantial enough to warrant further investigation. 9 references. (Author abstract modified)

185191 Al-Kaisi, A. H.; McGuire, R. J. Aramco Hospital, Dhahran, Saudi Arabia **The effect of sulthiame on disturbed behaviour in mentally subnormal patients.** British Journal of Psychiatry (London). 124:45-49, 1974.

Sulthiame was investigated as a tranquilizer in a double-blind trial on 34 severely subnormal patients with disturbed behavior. A special rating scale was used by nurses for the assessment of behavioral changes in hyperactivity, aggressiveness, destructiveness and antisociability. Results show that sulthiame was significantly effective in reducing disturbed behavior in general, and aggressiveness and hyperactivity in particular. Only one case of hyperpnoea was observed, in an epileptic patient. 7 references. (Author abstract)

185241 Sato, Eisuke; Nakane, Masafumi; Takahashi, Ryo. Department of Neuropsychiatry, Nagasaki University, School of Medicine, Japan **A case of periodic somnolence improved by the co-medication of L-dopa and methylphenidate.** Clinical Psychiatry (Tokyo). 15(8):900-903, 1973.

Successful treatment of a case of periodic somnolence with L-dopa and methylphenidate (MP) is discussed. The patient had an abnormal sense of depersonalization followed by somnolent seizure at age 19, and thereafter had a seizure once a month, sleeping intermittently for 6-10 days. No EEG abnormality or other organic disturbances were observed. Treatment with L-dopa began during the fifth seizure, but was unsuccessful. The patient was then treated with MP for 24 days, with no seizure occurring. Upon termination of MP the seventh seizure occurred and commencement of MP proved unsuccessful. The next seizure occurred 1 month later and treatment with both MP and L-dopa was begun. There was a marked decrease in the length of the seizure and further seizures were prevented for 4 months. 7 references.

185324 Rapoport, Judith L.; Quinn, Patricia O.; Bradbard, Gail; Riddle, K. Duane; Brooks, Elizabeth. Dept. of Pediatrics, Georgetown University Hospital, 3800 Reservoir Rd. N.W., Washington, DC 20007 **Imipramine and methylphenidate treatments of hyperactive boys: a double-blind comparison.** Archives of General Psychiatry. 30(6):789-793, 1974.

Imipramine and methylphenidate treatments of hyperactive boys are discussed, based on a double-blind outpatient study comparing imipramine hydrochloride, methylphenidate hydrochloride, and placebo treatments of 76 hyperactive grade school boys. Predrug behavioral evaluation is examined in detail to provide guidelines for clinics examining these children. Baseline clinic evaluations showed the usefulness of the psychologist's global estimates of attention and behavior disorder, as these ratings predicted teacher rating of classroom behavior better than did psychiatric playroom observations. Parent 4 day diaries of activity and family interaction also predicted teacher ratings and reflected response to stimulant medication. Although the global judgments of psychiatrists, psychologist, and the pediatrician indicated the superiority of both drugs to a placebo, all measures favored the stimulant drug. The significance of these findings may be limited, however, by the dose of imipramine hydrochloride (80mg), that was lower than in use elsewhere. 21 references. (Author abstract modified)

185330 Melges, Frederick T.; Tinklenberg, Jared R.; Deardorff, C. Melvin; Davies, Norma H.; Anderson, Richard E.; Owen, Catherine A. Dept. of Psychiatry, Stanford University School of Medicine, Stanford, CA 94305 **Temporal disorganization and delusional-like ideation: processes induced by hashish and alcohol.** Archives of General Psychiatry. 30(6):855-861, 1974.

Temporal disorganization and delusional like ideation were studied as processes induced by hashish and alcohol. From studies of acutely paranoid psychiatric patients, it was postulated that temporal disorganization might be involved in the emergence of delusional like ideation. To test this postulate, high doses of tetrahydrocannabinol were used to induce temporal disorganization in carefully screened normal subjects who had no detectable predisposition to delusional ideation. Each subject was used as his own control for five experimental conditions, including comparably intoxicating alcohol doses as well as placebo, at weekly intervals. Tetrahydrocannabinol conditions induced significantly greater temporal disorganization and delusional like ideation. For all subjects, there were substantial change correlations between temporal disorganization and delusional like ideation. Findings indicate that changes in the rate, sequence, and goal directedness of thinking processes were involved in the emergence of unusual thought content. 25 references. (Author abstract modified)

185600 Luria, Jeffry. City Univ. of New York **An investigation of interactions among LSD, dextroamphetamine, and verbal behavior in monologues and dialogues. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-Films, No. 74-10317 HC$10.00 MF$4.00 66 p.

The interactions among LSD, dextroamphetamine, and verbal behavior in monologues and dialogues were investigated. Classical approaches to drug research are examined, and a new model for such research is discussed. Recordings were made of patients under the influence of LSD, dextroamphetamine, and an inactive placebo, and comparisons of speech rhythms, specifically transitional pause probabilities, in monologues and therapeutic dialogues were made to test three hypotheses: 1) that there will be differences between monologues and dialogues; 2) LSD, which increases pauses in monologues, should be attenuated in respective dialogues, while dextroamphetamine, which decreases pauses in monologues, should be intensified in respective dialogues; and 3) both LSD and dextroamphetamine should decrease mean transitional pause probabilities. The three hypotheses were confirmed. The dichotomy between 'social' and 'personality' variables is examined and a different approach is suggested. (Journal abstract modified)

185604 McConahey, Ora Linda Schneider. Univ. of Minnesota **Effects of concurrent behavior modification and chlorpromazine administration in mentally retarded women. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-Films, No. 74-10544 HC$10.00 MF$4.00 159 p.

The relative contributions of chlorpromazine administration and operant conditioning methods in changing the behavior of 22 institutionalized mentally retarded women were compared. Procedures of the study are described, and the frequency of occurrence of 23 behaviors is analyzed. It is noted that no

behaviors recorded show significant chlorpromazine - placebo differences. It is suggested that operant conditioning techniques be used in preference to chronic chlorpromazine administration for behavior control. The results of the study cannot be extrapolated to high dosage chlorpromazine administration, nor does it preclude the use of phenothiazines in high dosages for psychotic patients or for chemical restraint. (Journal abstract modified)

185676 VanWyke, Paul Edward. Wayne State University **Dose effects of methylphenidate on behavioral inhibition and activation in hyperactive children. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-Films, No. 74-11175 HC$10.00 MF$4.00 166 p.

Acute (one hour) effects of varying doses of methylphenidate on behavioral inhibition and activation of hyperactive children were investigated. Hyperactive children were compared with a group of normal controls, on newly developed measures of behavioral inhibition and activation, to determine the degree to which the postulated behavioral deficits in this area were present in the experimental group. Dependent measures in the study are cited. Subjects were 21 hyperactive children and 18 controls, aged 5 years 8 months to 9 years. Hyperactive children were found deficient in patterning motor responses on tasks which require a continuous monitoring of a stimulus series, and/or which involve discriminant responding to certain stimuli. Attention was seen as a central component in the measured hyperkinetic behavioral deficit. It was found that methylphenidate results in improved attention to relevant cues and an increased ability for selective responding. Results support a low autonomic arousal hypothesis. (Journal abstract modified)

185715 Kreuter, Charles. California School of Professional Psychology **The effects of chlorpromazine on a redefined procedure of extinction of Sidman avoidance behavior. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-Films, No. 74-10680 HC$10.00 MF$4.00 184 p.

The effects of chlorpromazine (CPZ) on a redefined procedure of extinction of free operant (Sidman) avoidance without schedule correlated stimuli were studied. Performance under the redefined extinction contingencies was evaluated as a function of drug and nondrug conditions cited. It was found that the effect of CPZ on behavior generated under the redefined avoidance extinction schedule is dose related. The redefined extinction procedure was demonstrated to provide a sensitive measure for the evaluation of the effects of CPZ. Results are discussed in terms of methods of drug evaluation, state dependent learning, and usefulness of the redefined avoidance extinction procedure as an experimental analog for behavior therapy, especially flooding or implosive techniques. (Journal abstract modified)

185861 Aman, Michael G.; Sprague, Robert L. Department of Psychiatry, School of Medicine, Univ. of Auckland, Auckland, New Zealand **The state-dependent effects of methylphenidate and dextroamphetamine.** Journal of Nervous and Mental Disease. 158(4):268-279, 1974.

The effects of two stimulant drugs, Ritalin and Dexedrine, on both learning and retention were evaluated. The transfer effects which might result when the critical independent variable was the maintenance or change of the drug condition from learning to retention sessions were studied. The subjects were 18 hyperactive children who were put into one of the drug groups or in a control group. The subjects learned the tasks under their group drug condition and each was tested for retention under each of the possible drug conditions. Neither of the active drugs significantly improved learning or retention performance. Transfer appears to be as great when the drug conditions are changed as when they are maintained constant. 19 references. (Author abstract modified)

185881 Elliott, Henry W.; Gottschalk, Louis A.; Uliana, Regina L. Dept. of Medical Pharmacology and Therapeutics, College of Medicine, University of California, Irvine, CA **Relationship of plasma meperidine levels to changes in anxiety and hostility.** Comprehensive Psychiatry. 15(3):249-254, 1974.

Six adult male former drug users were given single 100mg doses of meperidine by the intramuscular route and an additional six were administered 100mg doses by the oral route in a single-blind situation. Anxiety and hostility were measured by speech content analysis before and after drug administration and correlated with plasma concentrations of meperidine. Significant decreases in anxiety and outward overt hostility scores occurred 1 to 1.5hr postdrug when plasma meperidine concentrations were high, with return of these affect scores toward predrug values at 6 hr when plasma concentrations of meperidine were falling. Meperidine was found to resemble sedative hypnotics in its effects on anxiety and hostility. Significant correlations were noted between plasma meperidine concentration and decrease in anxiety and hostility inward scores. The findings are consistent with the hypothesis that narcotic abuse is enhanced through the psychological effects of these drugs. 17 references. (Author abstract)

186395 Drakontides, Anna B. New York Medical College, Valhalla, NY **Drugs to treat pain.** American Journal of Nursing. 74(3):508-513, 1974.

Analgesics are analyzed to determine their use in relieving pain. It is noted that when analgesics are administered for pain relief, the underlying pathology remains. Narcotic analgesics are considered, including natural alkaloids present in opium, semisynthetic compounds obtained by relatively simple structural modifications of the morphine molecule, and synthetic compounds with structural resemblance to the morphine molecule. Factors considered include pharmacological differences, side-effects, and pain severity. Mild analgesics and their administration are also considered. The salicylates, paraaminophenols, and the pyrazolones with antipyretic and antiinflammatory actions are discussed. Combinations of analgesic drugs are reviewed. 25 references.

186643 Bergonzi, P.; Chiurulla, C.; Cianchetti, C.; Tempesta, E. Universita Cattolica del Sacro Cuore, Via della Pineta Sacchetti 526, 1-00168, Rome, Italy **Clinical pharmacology as an approach to the study of biochemical sleep mechanisms: the action of L-dopa.** Confinia Neurologica - Borderlands of Neurology (Basel). 36(1):5-22, 1974.

On the basis of clinicopharmacological and laboratory research, the action of L-dopa on sleep stages and sleep organization was examined. Patients suffering from Parkinson's disease were recorded before and after treatment with L-dopa, at various quantities of drug, throughout the night and during spontaneous sleep. In the basic night records a decrease in the 4th and rapid eye movement (REM) stages, and an increase of wakefulness. After average doses of L-dopa a decrease in wakefulness, a slight increase in slow sleep stages and a sharp rise in REM stage can be seen; moreover, the number of awakenings and the period for falling asleep are reduced. A higher dosage of the drug causes the alterations and the disturbances of the basic night recordings to reappear. 66 references. (Author abstract)

186744 Angrist, B.; Lee, H. K.; Gershon, S. New York University Medical Center, 550 First Ave., New York, NY 10016 **The antagonism of amphetamine-induced symptomatology by a neuroleptic.** American Journal of Psychiatry. 131(7):817-819, 1974.

The efficacy of the neuroleptic, haloperidol, in relieving the effects of amphetamine psychosis was evaluated. Haloperidol, in the doses used a specific blocker of dopamine, was effective in antagonizing amphetamine induced symptoms in eight patients. This finding suggests that dopaminergic mechanisms play an important role in amphetamine psychosis, as well as the additional possibility that these mechanisms may be important in other psychotic states. 13 references. (Journal abstract modified)

186833 Skorina, Jane Koepel. Wayne State University **A study of the effects of Ritalin intervention upon the perceptual competencies of children diagnosed as giving evidence of psychoneurological learning disabilities. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 74-11157 HC$10.00 MF$4.00 176 p.

The effects of Ritalin intervention on visual, auditory, and social perception for children diagnosed as psychoneurologically learning disabled were investigated. Data analysis failed to confirm the hypotheses relating to the influence of Ritalin intervention on visual, auditory and social perception. Ritalin intervention shows no significant relationship to perceptual patterns of children diagnosed as psychoneurologically impaired. Children labeled as psychoneurologically impaired when compared with normal children manifest differences in auditory, visual and social perception. It appears that the influence of Ritalin intervention on the psychoneurologically impaired is limited chiefly to the behavioral sphere. (Journal abstract modified)

187237 Fischer-Perroudon, C.; Mouret, J.; Jouvet, M. Hopital Neurologique, Universite Claude Bernard, 69 394, Lyon, France **/One case of agrypnia (4 months without sleep) in a Morvan disease: favorable action of 5-hydroxytryptophane./** Sur un cas d'agrrypnie (4 mois sans sommeil) au cours d'une maladie de Morvan. Effet favorable du 5-hydroxytryptophane. Electroencephalography and Clinical Neurophysiology. 36(1):1-18, 1974.

A case of agrypnia (4 months without sleep) in Morvan disease is described. The polygraphic recordings in the initial period confirmed the total insomnia. The patient was either under placebo or under 5-HTP treatment. Except for the fasciculations and distal paraesthesias, no obvious troubles were observed during daytime. In spite of total lack of sleep, the patient never felt sleepy or tired. None of the physical signs described during sleep deprivation experiments were noticed. Between 9 and 11 p.m.,dramatic hallucinatory episodes, accompanied by aggravation of distal pain and vasoconstriction, were regularly observed. These hallucinations were markedly enhanced by tryptophan loading, and disappeared under high doses of 5-HTP which restored normal sleep stages. 5-HTP given at large doses first improved the patient's condition dramatically. After 5-HTP withdrawal there was a gradual worsening of the patient's condition. 5-HTP therapy was again attempted but was then ineffective in reversing the symptoms and the patient died after 11 months of sickness. The neuropathology demonstrated no specific lesions. 53 references. (Author abstract modified)

15 TOXICOLOGY AND SIDE EFFECTS

182552 Yamanaka, Taeko; Mihara, Michiko; Sueta, Tazuko; Aoki, Noriko. Dept. of Ophthalmology, Tokyo Women's Medical College, Tokyo, Japan **The ocular complications by massive dose of psychotropic drugs.** Journal of Tokyo Women's Medical College (Tokyo). 41(11):842-847, 1971.

Twenty four patients with psychiatric disease were examined for ocular complications from treatment with phenothiazine derivatives and other psycholeptica. The maximum phenothiazine dosage was 2006g for 3 years. The lens opacities were shown on the interior surface and the pupillary area in seven cases with a large dose and long-term treatment. However, corneal change was seen in only one patient with lens opacity. No pigmentation was exhibited in the ocular fundi, skin and conjunctiva of all cases. Accommodation was disturbed as the antiadrenergic effect of psychotropica when the daily dosages were over 200mg, but elevation of ocular tension was not found. 13 references. (Author abstract modified)

182755 Konuma, Masuho. Hiroshima University, Hiroshima, Japan **Clinical studies of acute psychosis on the basis of chronic hypnotica intoxication -- an abstract report.** Japanese Journal of Studies on Alcohol (Kyoto). 7(1):21-25, 1972.

Acute neuropsychiatric symptoms observed in two patients suffering from barbiturate addiction are reported. Similarities to aftereffects of alcoholism are described. Disturbances included delirium tremens and pseudoparalysis. Neither patient used alcohol. (Author abstract modified)

182898 Roy, A.; Scherrer, P. no address **/Myocardiopathic complications induced by imipramine and tricyclic thymoleptics./** A propos des complications myocardiopathiques induites par l'imipramine et les thymoleptiques tricycliques. Annales Medico Psychologiques (Paris). 2(2):260-265, 1972.

Experiments with imipramine treatment and its toxic effects on the cardiovascular system are presented. Different opinions on its advantages and disadvantages are advanced based on several case histories. Imipramine can induce myocardiopathy and be otherwise patient if the doctor is not fully aware of the experimentation performed on imipramine treatment which still is in research stages.

183183 Harms, D. Kinderklinik der Universitat Erlangen-Nurnberg, Germany **/Somatic side-effects of psychotherapeutic drugs in childhood./** Somatische Begleiterscheinungen der Psychopharmakotherapie im Kindesalter. Klinische Padiatrie (Stuttgart). 185(3):172-180, 1973.

Somatic side-effects of psychotherapeutic drugs used in treating children are described. The more psychotropic drugs are used in children, the more frequent somatic side-effects will be found. Neurologic, central and peripheral autonomous, toxic, and allergic side-effects may occur under the treatment with antidepressives and major and minor tranquilizers. The main symptoms are dyskinesia, inhibition of the regulatory mechanisms of circulation, agranulocytosis, and allergic exanthema. Acute poisoning secondary to maternal ingestion of psychotropic drugs causes a depression of the vital functions of the neonate. After accidental ingestion of psychotherapeutic drugs, older children suffer from inhibitory effects on the central nervous system and disturbances of the cardial and central autonomous mechanisms governing circulation. Therapeutic necessities are discussed. 53 references. (Author abstract)

183200 Luyckx, A. Chaussee de Wez 3, B-5988 Nethen, Belgium **/Clinical experiment with a long-acting neuroleptic: fluspirilene (R6218)./** Experimentation clinique d'un neuroleptique a longue duree d'action: le fluspirilene (R6218). Acta Psychiatrica Belgica (Bruxelles). 72(6):748-755, 1972.

Fluspirilene(R-6218), a neuroleptic with a 7-day duration of action, was administered to patients divided into three groups, according to the type and length of the affection. These are respectively: long-term psychotics, recently affected psychotics and a small group of psychopaths and patients with below average IQ. Efficacy and type of side-effect in a clinical setting were tested. The most significant results are obtained in the incipient psychotic states, particularly when the autism is attended or accompanied by coenesthesic alterations of the body image. Results indicate frequent but benign side-effects. (Author abstract modified)

183749 Vichaiya, Vicharn. Somedet Chaopraya Hospital, Dhonburi, Bankok 6, Thailand **Side-effects of neuroleptic drugs.** Journal of the Psychiatric Association of Thailand (Bangkok). 15(3):210-227, 1970.

Side-effects encountered in the administration of neuroleptic drugs are reviewed. Effects manifested by disorders of the CNS, ANS, skin and eyes, blook, liver, and CVS are examined. Psychotoxicity, galactorrhea, edema, lactation, and oral moniliasis encountered with neuroleptics are reviewed. 18 references.

183786 Chapallaz, S. Centre Suissse d'Information Toxicologique a l'Institute de Medecine Legale, Universite de Zurich, Zurichbergstr. 8-8028 Zurich, Switzerland **/Acute poisoning by nitrazepam (MogadonR)./** Intoxications aigues par le nitrazepam (MogadonR). Bulletin de Medecine Legale et de Toxicologie Medicale (Lyon). 16(5):351-358, 1973.

Nitrazepam intoxication is examined. Nitrazepam is a nonbarbiturate sleeping medication producing a 6 to 8 hour sleep within 60 minutes. A brief description of its chemical structure, metabolism, mode of action, and side-effects is given. Poisonings by Mogadon associated with other medications or liquor and those solely by Mogadon are considered separately. Three hundred two cases are divided according to age, sex, and nature of intoxications. Different symptoms observed during simple poisonings include: neuropsychic signs; homodynamic signs; respiratory troubles; digestive troubles; allergic reactions; and metabolic troubles. Treatment methods are presented. Although the lethal dose of nitrazepam is not known, the presumed toxic dose is presumed to be between 1 and 2mg/kg. 21 references.

183812 Meyler, L.; Herxheimer, A. no address **Side effects of drugs.** Amsterdam, Excerpta Medica, 1972. 758 p. $42.50.

Side-effects of drugs are reviewed. Drugs used in psychiatry are considered under the following headings: central nervous system stimulants; antidepressive drugs; hallucinogens; hypnotics and sedatives; interneuron blocking agents; major tranquilizers; anticonvulsants; opioid analgesics; and narcotic antagonists.

184259 Solyom, Leslie; Kingstone, E. Allan Memorial Institute, McGill University, 1025 Pine Avenue West, Montreal 112, Quebec, Canada **An obsessive neurosis following morning glory seed ingestion treated by aversion relief.** Journal of Behavior Therapy and Experimental Psychiatry. 4(3):293-295, 1973.

The treatment of obsessive neurosis which developed following ingestion of morning glory seeds is described. Failure of other treatments (pharmacotherapy, psychotherapy) to effect any lasting improvement led to treatment with aversion relief therapy. A total of seven sessions eliminated the symptoms. At a 4 year followup he remains symptom free. 4 references. (Author abstract)

184436 Beumont, P. J. V.; Gelder, M. G.; Friesen, H. G.; Harris, G. W.; MacKinnon, P. C. B.; Mandelbrote, B. M.; Wiles D. H. Dept. of Psychiatry, Univ. of Cape Town, S. Africa **The effects of phenothiazines on endocrine function: I. patients with inappropriate lactation and amenorrhoea.** British Journal of Psychiatry (London). 124:413-419, 1974.

Fifteen female psychiatric patients who developed inappropriate breast activity and/or amenorrhea while receiving treatment with phenothiazines and related drugs were investigated. In the majority, plasma prolactin was clearly elevated. In those whose menstruation has not been affected, circulating level of luteinizing hormone (LM), immunoreactive estrogens (estradiol) and progesterone followed the normal pattern of the menstrual cycle. In amenorrheic subjects, basal LH values were variable, midcycle peaks absent, and estrogen and progesterone levels are similar to values reported during the follicular phase of a normal cycle. Medication was subsequently withdrawn from four patients. Termination of treatment reduced breast secretion and plasma prolactin fell to within the normal range, rising again when the drugs were reinstated. In two of three amenorrheic patients, withdrawal of medication led to a resumption of menstruation with a normal cyclical pattern of LH, estrogens and progesterone. 35 references. (Author abstract modified)

184439 Reynolds, E. H.; Travers, R. D. University Dept. of Neurology, Institute of Psychiatry and King's College Hospital Medical School, Denmark Hill, London, S.E. England **Serum anticonvulsant concentrations in epileptic patients with mental symptoms: a preliminary report.** British Journal of Psychiatry (London). 124:440-445, 1974

Serum anticonvulsant concentrations in epileptic patients with mental symptoms were examined. After excluding patients with signs of drug toxicity, mental symptoms preceding epilepsy, and evidence of a gross cerebral lesion, it was found that those patients with psychomotor slowing, intellectual deterioration, psychiatric illness or personality change have significantly higher serum DPH and phenobarbitone concentrations than those without such mental changes. Similar differences were found when those patients whose seizures were relatively well controlled were analyzed separately. The relationship between chronic anticonvulsant therapy and mental symptoms in epilepsy is briefly discussed, and the need for detailed study of this problem is emphasized. The value of serum anticonvulsant levels in detecting unsuspected drug toxicity, especially in brain-damaged mentally retarded patients, is confirmed. 22 references. (Author abstract modified)

185560 Ray, Aswini K.; Rao, Dodda B. Oak Forest Hospital, Oak Forest, IL **Calcium metabolism in elderly epileptic patients during anticonvulsant therapy.** Journal of the American Geriatrics Society. 22(5):222-225, 1974.

The possibility of hypocalcemia and osteomalacia in elderly epileptic patients on anticonvulsant drugs was studied. In none of the 36 patients did hypocalcemia develop. Serum phosphorus levels remained within normal limits, but alkaline phosphatase activity was slightly increased in 42% of the cases. It is concluded that hypocalcemia and osteomalacia, if

they do develop, are extremely rare in elderly epileptic patients who receive anticonvulsant therapy for short or long periods. In more than 90% of such elderly patients, a primary cause for the seizure disorder is obvious, and in more than two thirds of them the cause is cerebrovascular disease. 26 references. (Journal abstract modified)

186092 Pinkey, B. Severalls Hospital, Colchester, Essex, England **Psychiatric complications of everyday drugs.** Nursing Times (London). 70(20):756-757, 1974.

The side-effects of drugs prescribed for their action on the central nervous system (CNS), which may produce psychiatric symptoms, are described. Drugs whose possible side-effects are described are: CNS stimulants and antidepressants, CNS depressants, analgesics and antipyretics, autonomic drugs, drugs acting on the cardiovascular system, antiinfective drugs and steroids are considered. It is noted that certain drugs may produce unexpected secondary effects -- psychiatric symptoms. It is suggested that nurses attending patients who have been prescribed such drugs be alert to any signs of unexpected mental change and report such signs to the doctor.

186204 Story, Norman L. Counselling Center, Univ. of Northern Iowa, Cedar Falls, IA 50613 **Sexual dysfunction resulting from drug side effects.** Journal of Sex Research. 10(2):132-149, 1974.

Brand name drugs (118) that have sexual side effects are cited. These drugs (primarily psychotropic) are presented in chart form for easy reference. In Section I, drugs are listed alphabetically by name, along with the sexual side effects, and possible medical use. Section II lists alphabetically, the generic and chemical names of the brand name drugs found in the first section. Drugs used in the study are classified as: antihypertensive, antihypertensive with a diuretic combination, antianxiety, antidepressant, antipsychotic, or anorexic. 38 references. (Author abstract modified)

186473 Franklin, L. M. Southland Hospital, Invercargill, New Zealand **Thyrotoxicosis developing during lithium treatment: case report.** New Zealand Medical Journal (& Supplement) (Dunedin, New Zealand). 79(511):782, 1974.

A case report of a woman who developed thyrotoxicosis in the fourth year of lithium treatment is presented. It is widely accepted that lithium treatment can disturb thyroid function and cause a goiter; most affected patients remain euthyroid although a few develop hypothyroidism, but toxic goiter had not hitherto been reported. In the case provided there is no proof that lithium caused the thyrotoxicosis. 4 references. (Author abstract modified)

187254 Martin, William R.; Thompson, William O.; Fraser, Havelock F. National Institute on Drug Abuse, Addiction Research Center, Lexington, KY **Comparison of graded single intramuscular doses of morphine and pentobarbital in man.** Clinical Pharmacology and Therapeutics. 15(6):623-630, 1974.

Graded single intramuscular doses of morphine sulfate (8, 16, and 32mg) and pentobarbital sodium (150, 200, and 250mg) were compared. The various doses of the drug and a placebo were administered double-blind to 12 nontolerant narcotic addicts. To assess the magnitude and time course of subjective effects and associated signs, single and chronic dose opiate questionnaires were completed by subjects and observers. Objective measurements of drug effect were concurrently made, using photographs of the pupils and the duration of postrotational nystagmus. Overall, the questionnaires showed definite and different constellations of symptoms and signs for morphine and pentobarbital. Morphine induced a dose related decrease in pupillary diameter and an increase in the signs scratching, relaxed, coasting, talkativeness, and conjuctival injection and caused relaxation, talkativeness, and turning of the stomach. Pentobarbital induced a dose related increase in the duration of postrotational nystagmus and caused sleepiness and drunkenness. 14 references. (Author abstract modified)

187256 Gorodetzky, Charles W.; Kullberg, M. Peter. National Institute on Drug Abuse, Addiction Research Center, Lexington, KY **Validity of screening methods for drugs of abuse in biological fluids. II. Heroin in plasma and saliva.** Clinical Pharmacology and Therapeutics. 15(6):579-587, 1974.

In a study of the validity of screening methods for drugs of abuse in biological liquids, five subjects received three single intravenous doses of heroin, 2.5, 5, and 10mg per 70 kg and 1 oral dose of dextromethorphan, 60mg per 70 kg; another four subjects received morphine, 30mg, subcutaneously, four times per day for 3 months. Saliva and plasma samples were collected at intervals for 48 hours following each single drug dose and hourly for 6 hours between chronic doses. Plasma samples were analyzed for opiate by RIA, and saliva samples by radioimmunoassay, a modified free radical assay technique (FRAT), and the homogeneous enzyme immunoassay technique (EMIT). The low dose of heroin was not consistently detectable at any sampling time in either the plasma or the saliva. The medium and high doses were detectable with high probability for 24 hours in plasma and 12 hours in saliva. Dextromethorphan was not detectable in plasma but was detected with high probability in saliva for 30 minutes by EMIT and 2 hours by FRAT. During chronic administration there were high probabilities of detection of morphine in plasma for at least 6 hours and in saliva for 3 to 4 hours after the last morphine dose. While these fluids do not appear to be as useful as urine in routine screening for heroin, they may be useful in the detection of high dose chronic abuse. 17 references. (Author abstract)

16 METHODS DEVELOPMENT

185977 Martis, Leo; Levy, Rene H. Dept. of Pharmaceutical Sciences, School of Pharmacy, Univ. of Washington, Seattle, WA 98195 **GLC determination of meprobamate in water, plasma and urine.** Journal of Pharmaceutical Sciences. 63(6):834-837, 1974.

A GLC method for the determination of meprobamate in water, plasma and urine is described. The procedure is based on alkaline hydrolysis of meprobamate followed by silylation of the hydrolysis product to give a trimethylsilyl derivative. Quantitation of the drug was effected using a homolog of the hydrolysis product as an internal standard, which is also silylated during the procedure. The method is specific, sensitive and reproducible and has been used for the routine analysis of biological samples obtained from meprobamate treated dogs and humans. 29 references. (Author abstract)

186566 Fri, Claes-Goran; Wiesel, Frits-Axel; Sedvall, Goran. Department of Pharmacology, Karolinska Institutet S-104 01 Stockholm 60, Sweden **Mass fragmentographic analysis of homovanillic acid and its homoiso analogue in cerebrospinal fluid using the alpha-dideutero acid as internal standard.** Psychopharmacologia (Berlin). 35(4):295-304, 1974.

The preparation and use of homovanillic acid (HVA)-d2 for the mass fragmentographic determination of HVA levels in the cerebrospinal fluid (CSF) is described. Following extraction

and synthesis of the methyl ester heptafluorobutyryl derivatives samples were injected into a combined gas chromatograph - mass spectrometer connected to a multiple ion detector. The two fragments set into focus were the molecular ions of authentic HVA and HVA-d2 respectively. The experimental error was less than 4%. The recovery of small amounts of authentic HVA added to CSF was satisfactory. Multiple ion determination using two sets of fragments gave similar results demonstrating high specificity and reproducibility of the method used. The mass spectral characteristics of the methyl ester heptafluorobutyryl derivative of ISO-HVA suggested that this compound could be differentiated from HVA by mass fragmentography. Thus the base peak did not constitute the molecular ion in the spectrum of the ISO-HVA derivative as it is for the derivative of HVA. Multiple ion analysis of CSF before and after the addition of ISO-HVA failed to supply positive evidence for the presence of ISO-HVA in CSF in neurological or schizophrenic patients. 14 references. (Author abstract)

17 MISCELLANEOUS

182574 No, Yeong Il; Han, Dong Se. Department of Neuropsychiatry, Seoul National University College of Medicine, Seoul, Korea **Clinical study of tranquilizers.** Korean Central Journal Of Medicine (Seoul). 18(1):27-28, 1970.

Clinically tested major and minor tranquilizers are examined. Rauwolfia derivatives (major tranquilizers) which suppress sensory organs by separating serotonin from the brain are studied and include: reserpine, deserpidine, rescinnamone, sirosingopine, rauwolfia root, and alseroxylon. The minor tranquilizers investigated are chemically different from the major tranquilizers and are also different in pharmacological operation, applicability, and side-effects. They can be used as a supplement to normal psychiatric treatment. The minor tranquilizers discussed are: meprobamate, chlordiazepoxide, and diazepam. 6 references.

182761 Penn, R. G. Winthrop Laboratories, Surbiton-upon-Thames, Surrey, England **The basic pharmacology of oxypertine.** Postgraduate Medical Journal (Oxford). 48(Suppl. 4):7-11, 1972.

The pharmacology of oxypertine was discussed in a symposium held at Cambridge in 1972, on the pharmacology and clinical use of oxypertine in anxiety including its development, structural properties, and action. Oxypertine is an indole derivative with a phenyl piperazine side chain to facilitate passage of blood - brain barrier. Oxypertine is similar to chlorpromazine in effect, potentiating central depressant actions. In monkey, oxypertine is twice as effective in action on taming, depression and catatonia as chlorpromazine. Oxypertine's biochemical action is in lowering the noradrenaline content of rat brain very rapidly and depression of the CNS. Monoamine oxidase inhibitors prevent the decline in brain adrenaline and noradrenaline caused by oxypertine. Like reserpine, oxypertine stimulates the release of the catecholamines from the subcellular storage vesicles and inhibits their reuptake. Differences in the action of oxypertine and reserpine are discussed. Catecholamines and their metabolites are greatly increased in blood and urine in times of stress and anxiety, and thus the action of oxypertine as an antianxiety drug is considered. 11 references.

182770 Berger, F. M. Wallace Labs, Cranbury, NJ **Social implications of psychotropic drugs.** In: Garattini, S., Advances in Pharmacology and Chemotherapy. New York, Academic Press, 1972. 432 p. (p. 105-118), v. 10.

The social consequences resulting from the use of psychotropic drugs in the medical treatment of mental illness are evaluated. Epidemiological data were examined to see if these drugs were socially beneficial and whether their use was reflected in changes in the population of mental hospitals or in the incidence of suicide. Other aspects investigated whether the use of these substances cause damage to society by impairing initiative, performance and creativity of the individual. The possibility that these substances can control the mind is investigated as well as possible dependency and likelihood of inducing social or dangerous behavior in users. 31 references.

182771 Schallek, William; Schlosser, Walter; Randall, Lowell O. Dept. of Pharmacology, Research Div., Hoffmann-La Roche Inc., Nutley, NJ **Recent developments in the pharmacology of the benzodiazepines.** In: Garattini, S., Advances in Pharmacology and Chemotherapy. New York, Academic Press, 1972, 432 p. (p. 119-183), v. 10.

The pharmacology of the benzodiazepines is discussed based on articles published between 1967 and 1971. Evidence is given that the depressant effects on the central nervous system may be caused by release from inhibition. Other developments covered include: the mechanism of the muscle relaxant effects, evidence for sites of action in the brain, studies on the metabolism of these compounds, anticonvulsant activity, behavioral effects, neuropharmacology and biochemical effects. The following benzodiazepams are covered: chlordiazepoxide HCl, diazepam, oxazepam, medazepam HCl, flurazepam HCl, bromazepam, nitrazepam, clonazepam and flunitrazepam. 136 references. (Author abstract modified)

182772 McClure, William O. Dept. of Biochemistry, Univ. of Illinois, Urbana, IL **Effect of drugs upon axoplasmic transport.** In: Garattini, S., Advances in Pharmacology and Chemotherapy. New York, Academic Press, 1972, 432 p. (p. 185-220), v. 10.

Axoplasmic transport relevant to the action of several psychoactive agents is considered. Drugs examined in the context of axoplasmic transport include: tranquilizers, antimitotic agents, methoxylated phenylalkylamines, anesthetics, aluminum ions and neuropathic agents. 155 references.

182773 Lemberger, Louis, Dept. of Pharmacology and Med., Indiana Univ. School of Med., Indianapolis, IN **The metabolism of the tetrahydrocannabinols.** In: Garattini, S., Advances in Pharmacology and Chemotherapy. New York, Academic Press, 1972, 432 p. (p. 221-255), v. 10.

A review of the literature on the metabolism of the tetrahydrocannabinols is presented which includes the following topics: nonenzymic transformations of cannabinoids; in vitro metabolism of tetrahydrocannabinols; in vivo studies with delta9-tetrahydrocannabinol including absorption, dispostion, excretion and metabolism; factors affecting delta9-tetrahydrocannabinol including stimulation, inhibition and sex difference; pharmacological activity: delta9-tetrahydrocannabinol versus an active metabolites in biological fluids; and biochemical correlates of clinical findings, specifically, tolerance versus reverse tolerance and spontaneous recurrence of flashback. 142 references.

182835 Thomas, Molly. Department of Pharmacology, Christian Medical College, Vellore, India **Drugs acting on the central nervous system.** Indian Journal of Hospital Pharmacy (New Delhi). 9(2):49-60, 1972.

Tranquilizers, antianxiety agents, antidepressants, sedatives, hypnotics, analgesics, and anorexiants which operate on the central nervous system are examined. Major characteristics, side-effects, adverse reactions, and precautions are listed for each drug. Generic and trade names are given. Usual dosages and forms of availability are given.

182870 Nagaraja, Jaya. Community Mental Health Centre, Banjara Hills, Hyderabad, India **Somnambulism in children -- clinical communication.** Child Psychiatry Quarterly (Hyderabad). 7(1):18-19, 1974.

Two cases of somnambulism in school aged children are described. Patients were an 8-year-old boy with no neurotic traits or psychotic trends and a 9-year-old girl whose sleep walking was associated with separation anxiety and mild depression. Both children were successfully treated with chlorpromazine. 2 references.

182899 Scherrer, P.; Quiniou-Vidalenc; Maillard, M.; Roy, J.-C no address **/Importance of the cooperation of families in the treatment of the sick: concerning chronic delirium treated with neuroleptics and melancholy treated with antidepressants./** De l'importance de la cooperation des familles au traitement des malades: a propos d'une delirante chronique traitee par les neuroleptiques et d'un melancolique traite par les antidepresseurs. Annales Medico Psychologiques (Paris). 2(2):266-271, 1972.

Two case histories and their treatment in a family perspective are discussed: one of a woman suffering from chronic delirium, and the other of a man suffering from despondance and suicidal tendencies. The woman's family suggested her hospitalization in hopes that it would cure her. At first she saw it as a rejection but gradually with the help of incisive neuroleptics, she was practically cured of her delirium. In the second case the wife of the man in question grew increasingly impatient to have him 'cured'. He had begun to respond to treatment with Tofranil, Nozinal, and tranquilizers. His wife sought out another doctor, known for his cures, to speed up the complete recovery of her husband. This doctor prescribed the cessation of the antidepressant and neuroleptic treatments. After approximately 10 days, the patient committed suicide.

183521 Arushanyan, E. B. Department of Pharmacology, Chitinsky Medical Institute, Chita, USSR **/Antipsychotic action of neuroleptic agents and the function of basal ganglia (survey of literature)./** Antipsikhoticheskoye deystviye neyroleptikov i funktsiya bazal'nykh gangliyev (obzor literatury). Farmakologiya i Toksikologiya (Moskva). 36(4):481-489, 1973.

The antipsychotic effect of neuroleptics and the function of basal ganglia were studied. Experimental symptoms suggest examination as an indicator of expected clinical results. A breakdown of psychic and motor movements under the influence of neuroleptics suggests a common origin which can be attributed to basal ganglia. 140 references.

183544 Dufrasne, M. no address **/A summary of the clinical dossier on depamide./** Synthese du dossier clinique actuel du depamide. Feuillets Psychiatriques de Liege (Liege). 5(1):77-80, 1972.

Animal and human experiments with depamide are summarized. Anticonvulsive and toxicological findings in animals are reviewed. A double-blind study using 300mg of the drug for 24 hours on a control group of healthy persons showed a higher score on performance tests, an increase in phases III and IV of sleep with a decrease of P.M.O. on the EEG, and a desynchronization of the alpha rhythm on the EEG; no adverse effects were noted. Tests on epileptics showed a stabilization of humor, a toning down of euphoric or depressive tendencies, and a reduction or even disappearance of impulsiveness. The use of the drug by itself on patients with a manic-depressive psychoses showed no effect; however, when used as an adjuvant with neuroleptics (manic states) or antidepressants (depressive states) the use of depamide permits a decrease in the dosages of the other drugs. Only two adverse effects to depamide are noted and they occur rarely: digestive troubles and very exceptionally in the case of an older patient a confusional fit may occur. Long and consistent treatment with heavy doses is necessary as the drug is very slow acting.

183630 Venables, Peter H. Dept. of Psychology, Birkbeck College, University of London, Malet St., London, WC1 E7HX, England **Comments on paper, 'Psychophysiological patterns of response in schizophrenia'.** Journal of Nervous and Mental Disease. 158(2):115-117, 1974.

The value of studying schizophrenics under treatment with phenothiazines in an attempt to assess the underlying mechanism of schizophrenia is discussed. Three research strategies are examined: 1) premorbid state; 2) experimentally modulated dosages of phenothiazines; and 3) the patient as is under phenothiazine medication. Only the third approach is practical and ethically permissable. Research done prior to advances in psychopharmacology and current studies on drugged patients provide a viable and meaningful approach to studying the schizophrenic. 6 references.

183635 Newmark, Charles S.; Dinoff, Michael; Raft, David. Dept. of Psychiatry, University of North Carolina Medical School, Chapel Hill, NC 27514 **The standardized video-tape interview as an objective dependent variable in psychotropic drug research.** Journal of Nervous and Mental Disease. 158(1):18-24, 1974.

Literature on the development and present status of the standardized videotape interview is reviewed. Since this interview technique shows promise of being a highly reliable and clinically valid instrument for assessing clinical changes in a behavioral, objective and parsimonious manner, and because of its demonstrated ability to reflect meaningful change based on specific experimental and therapeutic conditions, it would seem to be a useful dependent variable in psychotropic drug studies. 50 references. (Author abstract)

183693 Jus, A.; Jus, K. Departement de psychiatrie, Faculte de medecine, Universite Laval, Quebec 10, Canada **/Neurophysiological research in psychiatry and its relationship to psychopharmacology./** La recherche neurophysiologique en psychiatrie et ses relations avec la psychopharmacologie. Vie Medicale au Canada Francais (Quebec). 2(10):965-974, 1973.

The role of neurophysiology in the evolution of clinical psychopharmacology is examined. Such clinical neurophysiological methods and techniques as polygraphic registrations, simple reactivity studies, and qualitative and quantitative computer analysis of data have provided important psychopharmacological information. Data pertaining to the prognosis of psychiatric disorders are particularly important to the prediction of therapeutic effects, the nature of cortical, autonomic, and skeletomuscular conditional reactions, and the mechanisms of action of neuroleptic, antidepressant, hypnotic and psychotomimetic drugs. Neurophysiological data should be correlated with a detailed psychopathological analysis in each case. 77 references. (Journal abstract modified)

183706 Aleksandrowicz, Malca K. 1933 Burnett Rd., Topeka, KS 66604 **The effect of pain relieving drugs administered during labor and delivery on the behavior of the newborn: a review.** Merrill-Palmer Quarterly of Behavior and Development. 20(2):121-141, 1974.

The effects of drugs given during labor and delivery upon the behavior of the neonate are outlined. Since psychologists have a growing interest in neonatal behavior but lack a background of experience in the administration of drugs or a full understanding of their effects, the following topics are reviewed: the drugs commonly used during labor and delivery, the methods of administration, the metabolism of the drugs, the process of placental transfer, and the effect of the drugs on the different organs and systems of the fetus. In addition, the literature dealing with the influence of drugs on the behavior of the neonate is reviewed with particular emphasis on the infant's 'social' behavior. 68 references.

184322 no author. no address **Second minor tranquilliser on pharmaceutical benefits list.** Health (Canberra). 23(2/3):23,1973.

The placing of several drugs, including oxazepam, on the Australian pharmaceutical benefits list is reported. Drugs on this list can be prescribed without prior authorization of the Directors of Health in the States. Drugs discussed include: oxazepam (Serepax), a minor tranquillizer; prochlorperazine maleate (Stemetil) and thiethylperazine (Torecan), preparations for the treatment of Meniere's syndrome which is characterized by severe bouts of vertigo and vomiting; Salbutamol, which is used to dilate the bronchial tubes during asthmatic spasms; and two antibiotic ointments, chlortetracycline (Aureomycin) and oxytetracycline (Terramycin).

184630 Cole, J. O.; Freedman, A. M.; Friedhoff, A. J. no address **Psychopathology and psychopharmacology.** Baltimore, Johns Hopkins Press, 1973. 298 p. $15.00.

Papers presented at the 62nd Annual Meeting of the American Psychopathological Association in 1972 are reported. This reference source of technical material deals with drug models of schizophrenia, clinical and basic research on drugs and psychopathology, and a special lecture on drugs and society. Instrumentation of drug models of psychoses includes work with humans and animals.

184803 Morris, Jeffery B.; Beck, Aaron T. Hahnemann Medical College, Philadelphia, PA **The efficacy of antidepressant drugs: a review of research (1958 to 1972).** Archives of General Psychiatry. 30(5):667-674, 1974.

An extensive review of publish research on the efficacy of antidepressant medication is presented. Inconsistencies of previous reviews are overcome by the inclusion of 146 double-bline studies on medications actively promoted in the U. S. as antidepressants during 1972 as well as on lithium carbonate and five other drugs not promoted as antidepressants. Results show tricyclic antidepressants to be significantly more effective than a placebo in 61 of 93 group comparisons. No study reported a placebo as more effective than a tricyclic. The two monamine oxidase inhibitors that were actively marketed as antidepressants in the U.S. were significantly more effective than a placebo in 8 or 13 comparisons. Lithium carbonate was not conclusively shown to be an effective antidepressant on the basis of eight double-bind reports. 185 references. (Author abstract modified)

184955 Scelles, F.; Mahuzier, G.; Saby, J.; Borenstein, P. Laboratoire Central, Hopital psychiatrique de Villejuif, 54, avenue de la Republique, 94800 Villejuif, France /**Indications and dosage for maximal activity of ornithine-carbamyl-transferase in the psychiatric environment.**/ Interet et dosage de l'activite de l'ornithine-carbamyl-transferase en milieu psychiatrique. Annales Medico Psychologiques (Paris). 1(2):183-193, 1974.

Measurement of ornithine-carbamyl-transferase activity (OCT) in determining the effects of certain treatments and drugs on the liver is discussed. The sensitivity of the OCT can in effect show that the changing of a treatment or more simply the modification of a dosage can be felt by the hepatic cell in certain subjects. An increase in the activity of the OCT can also be incurred by drug abuse or alcoholism. It is concluded that analyses of this type may be more successful than the traditional investigations in the exploration of the effects of certain treatments. 8 references. (Journal abstract modified)

184959 Soubrier, Jean-Pierre. Clinique Toxicologique, Hopital Fernand-Widal, Service du P. M. Gaultier, Universite Paris VII, Paris /**Chemotherapy and psychotherapy, are they complementary or antagonistic?: a personal study.**/ Les chimiotherapies et les psychotherapies sont-elles complementaires ou antagonistes? (A propos d'une etude personnelle). Annales Medico Psychologiques (Paris). 1(2):225-233, 1974.

Present chemotherapeutic and psychotherapeutic methods are considered from a suicide prevention perspective. Based on a survey, it is shown that 80% of the admissions for intoxication are attributable to psychotropes. Based on the facts presented it is concluded that even though the psychotropes are said to permit a reduction in the number of suicides, they do not reduce the number of potential suicides.

184961 Sizaret, P.; Degiovanni, A. no address /**A case of tardive dyskinesia appearing precociously under neuroleptics.**/ Un cas de syndrome dyskinetique dit tardif apparu precocement sous neuroleptiques. Annales Medico Psychologiques (Paris). 1(2):247-249, 1974.

The observation of a patient presenting a type of dyskinesia which detached itself from classic manifestation by its early appearance and evolution but with typical symptomatology is described. The effects of certain neuroleptics such as Lithium Carbonate, Pipothiazine, and Benzodiazepine are described. It is concluded that the case is quite exceptional, and therefore no opinions concerning the pathogenesis of the troubles are permitted. 6 references.

185182 Sano, Isamu. Osaka University, Japan **Treatment of mental disorders.** Popular Medicine (Tokyo). 50:98-100, 1973.

Psychopharmacological treatment of mental disorders is considered. Improved therapy has enabled more patients with severe mental illness to function in society. Two major problems are: 1) the tendency of patients to become dependent on drugs; and 2) the possibility for mental patients to marry and produce mentally deficient children. It is felt that development of eugenics must be considered. The recent discovery of a relationship between endogenous mental illness such as manic depression and schizophrenia, and brain metabolism is discussed.

185195 Ballinger, Brian R. Royal Dundee Liff Hospital, Liff, by Dundee, DD2 5NF, Angus, Scotland **The discharged patient's drug treatment.** British Journal of Psychiatry (London). 124:60-63, 1974.

The quality of information regarding drug treatment sent to general practitioners at the time of a patient's discharge from a psychiatric hospital, and the proportion of patients remaining on psychotropic drugs 18 months after discharge were surveyed. The drug treatment recommended in the discharge letters of 359 psychiatric patients was compared with the records of the supply of drugs given on leaving the hospital, and differences were found in 20.6% of the sample. A comparison of the patients' treatment sheets, and the records of drugs given on leaving the hospital shows that drugs had been discontinued on the day of discharge in 26.4% of the total. It is suggested that the communication of information about drug treatment to general practitioners requires further attention, and that drugs should not be discontinued on the day of discharge. It was also found that 49.1% of the patients were still receiving psychotropic drugs 18 months after discharge and that only 35.3% of these prescriptions were for drugs of the same group as those given at the time of discharge from the hospital. 3 references. (Author abstract modified)

185235 Hozaki, Hideo. Keio Gijuku University, Japan **Control of mental activities.** Popular Medicine (Tokyo). 50:35-38, 1973.

Psychopharmacology in controlling mental activities is reviewed. Psychotropic drugs which affect human emotions, volition and desire, memory and cognition, and personality, and their mechanism of action are considered.

185350 Ogawa, Nobuya. Department of Pharmacology, Faculty of Pharmaceutical Sciences, Kyushu University, Japan **Clinical evaluation of anxiolytic drugs.** Journal of Japanese Psychosomatic Society (Tokyo). 13(4):241-244, 1973.

The methodology for screening anxiolytic drugs adopted by the U.S. Food and Drug Administration is outlined. Various levels of screening are reviewed. 5 references.

185898 DiMascio, Alberto; Goldberg, Harold. Dept. of Psycopharmacology, Massachusetts Dept. of Mental Health, Boston, MA **Drug dosage in acute-phase schizophrenia.** Hospital Physician. 10(5):71, 1974.

The drug dosage in acute phase schizophrenia is outlined. The chemical class, the names of commonly used drugs and daily dosage is tabulated. The drugs are phenothiazines, butyrophenones and thioxanthenes.

186474 Howard-Jones, Norman. no address **Man and his medicines.** World Health. April:4-11, 1974.

A historic review of the uses of drugs and chemicals to heal the sick is presented. Until recent decades, men have tried to cure all ills by ingesting or applying externally various chemical, plant, or animal concoctions which usually had no medicinal value. Not until the early Nineteenth century did chemists begin isolating the active principles in drugs. The history of synthetic drugs and chemotherapy are included.

187022 Lader, Malcolm. no address **Institute of Psychiatry Clinical Psychopharmacology Research Team.** Psychological Medicine (London). 4(1):110-116, 1974.

The Clinical Pharmacology Research Unit at the Institute of Psychiatry is described. The aims and strategies of the unit are presented. The development and evaluation of new techniques are outlined. The factors governing the habituation of the galvanic skin response (GSR) and the influences of attention activation and interstimulus interval on the auditory evoked potential have been studied. Patients with anxiety states were compared to normal Ss and were found to have higher skin conductance levels, more skin conductance variability and slower habituation of the GSR. Depressed patients were found to have excessive sweat gland activity. In a study of depressed patients, sweat gland activity was excessive in agitated patients and almost absent in retarded ones. The roles of amylobarbitone, chlordiazepoxide, chlorpromazine and beta-blocking agents on depression were also examined. Antidepressants and tryptophan were also investigated from a clinical point of view. 52 references.

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